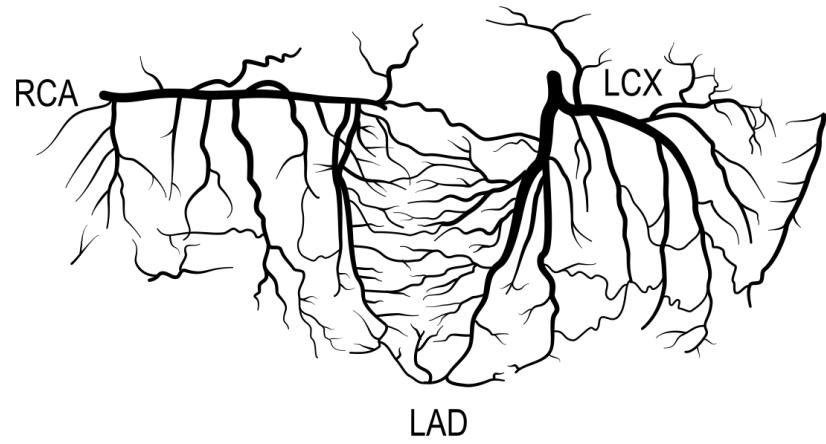


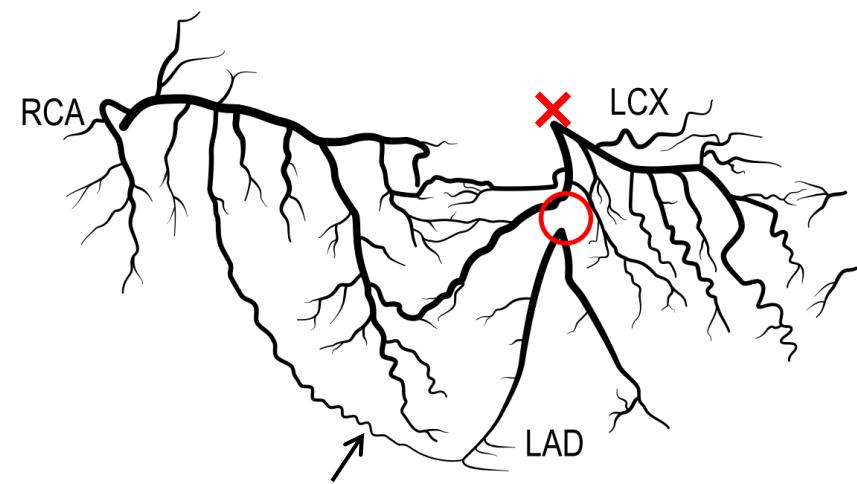
Protective Effect of the Human Coronary Collateral Circulation

Christian Seiler, Bern, Switzerland
No conflicts of interest to disclose

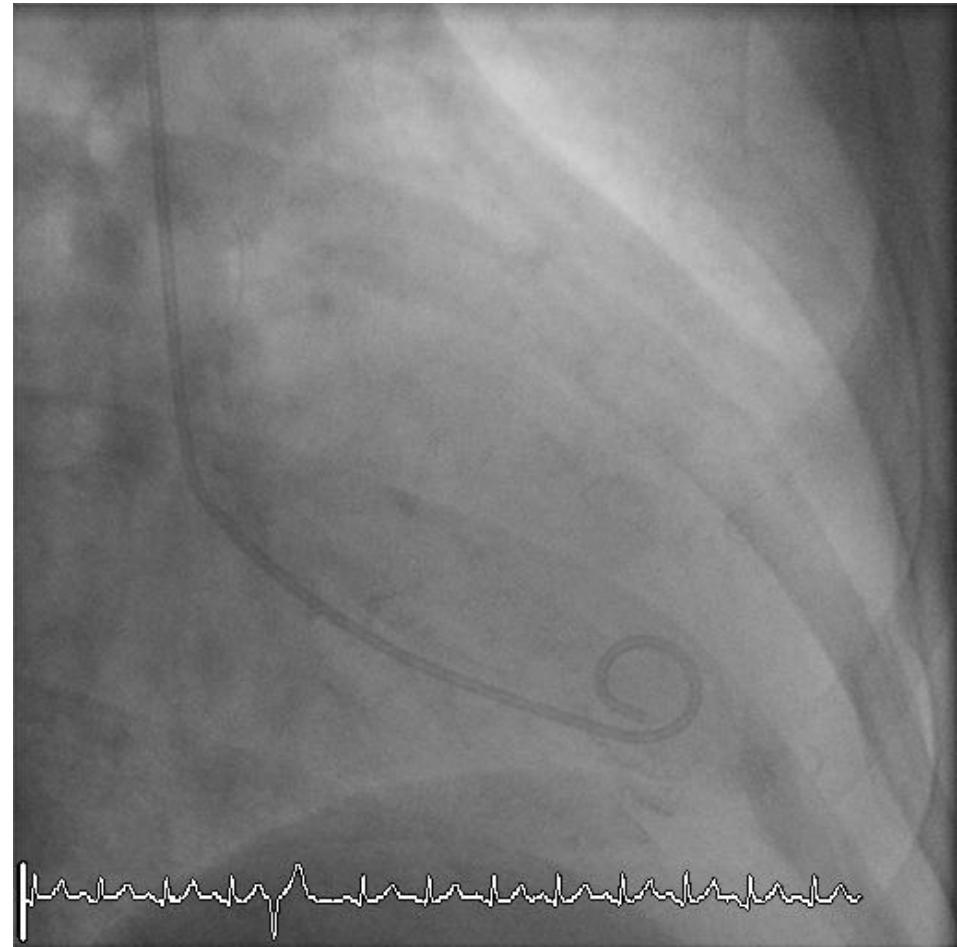
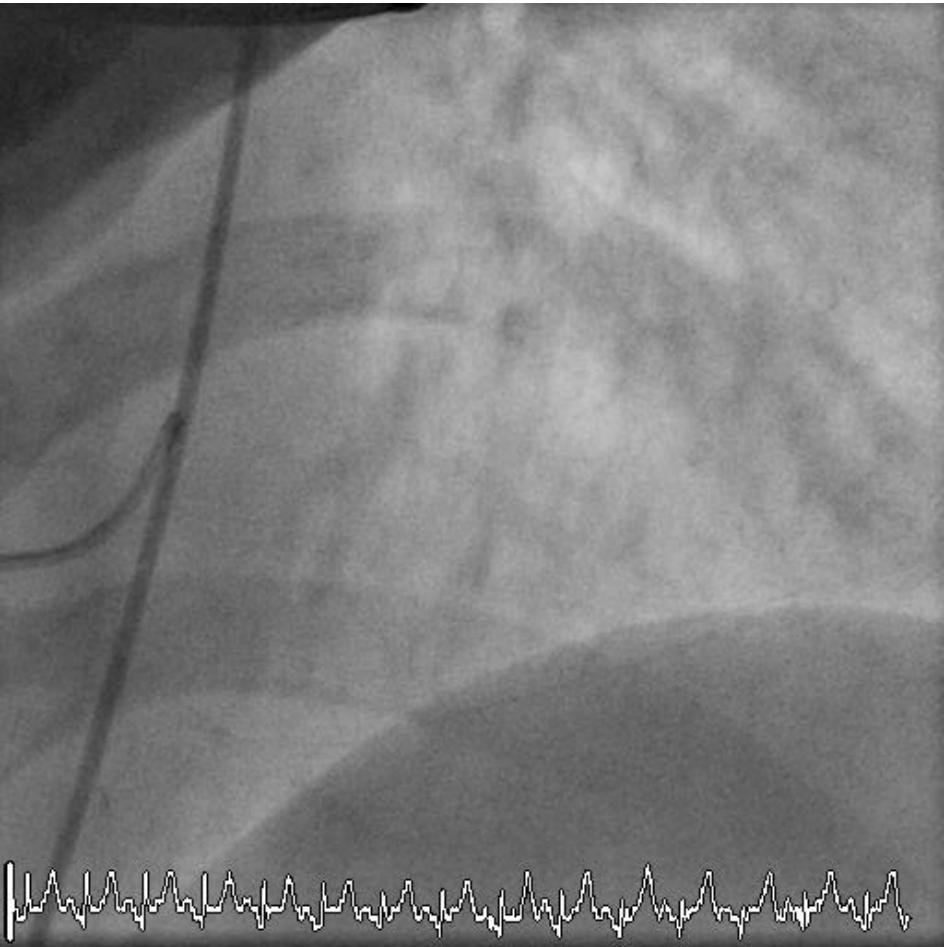
Normal heart

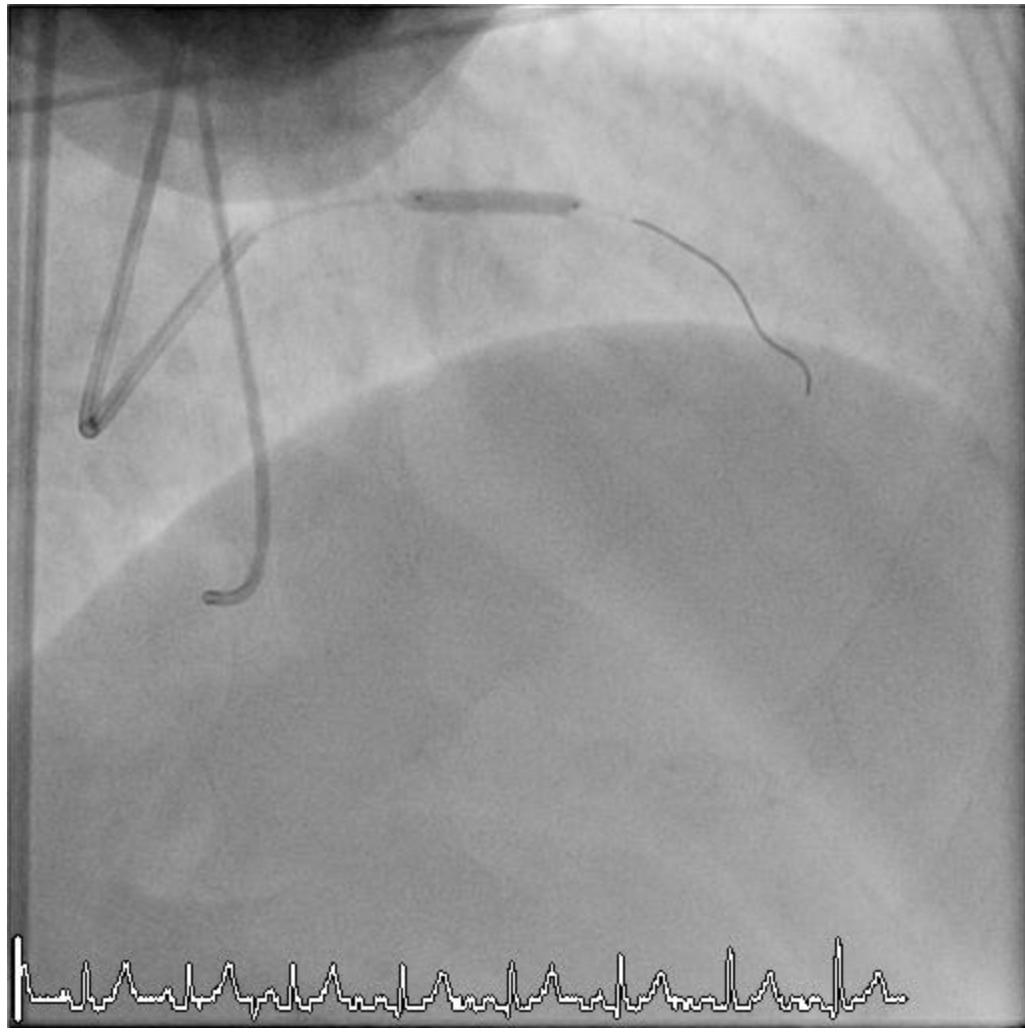


Occlusive CAD



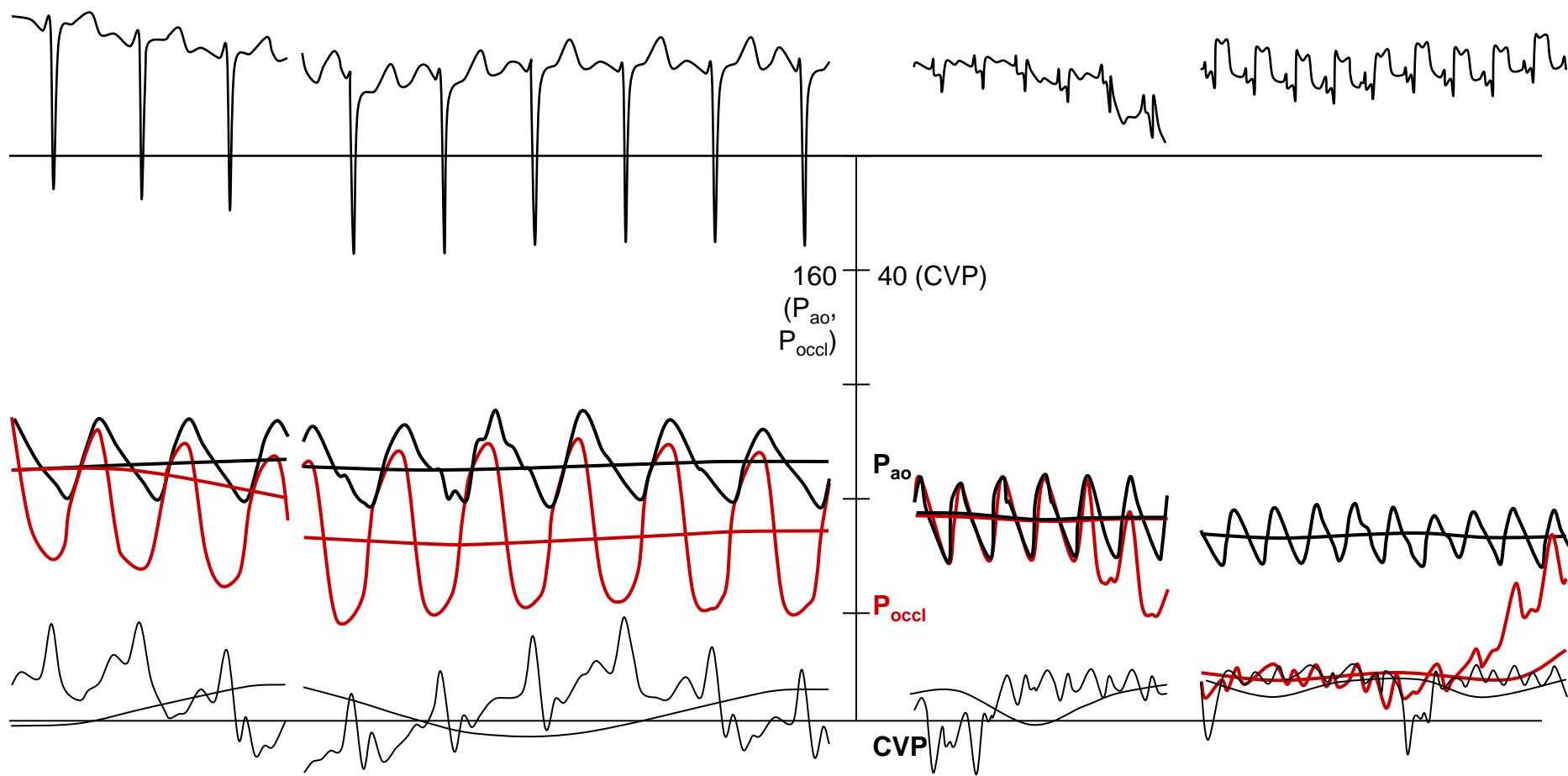
Fulton. Brit Heart J 1964; 26: 1-





Patient A

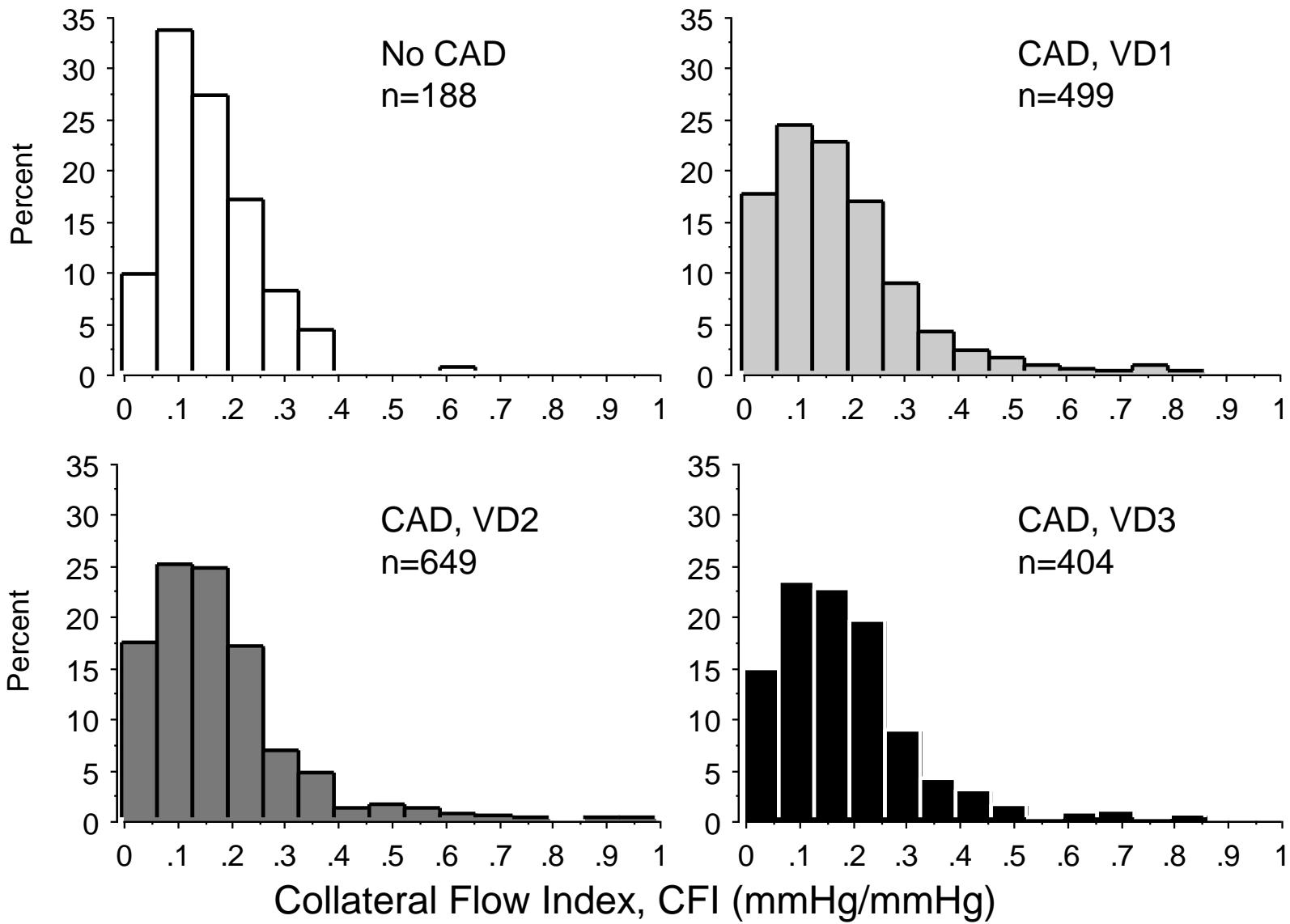
Patient B



$$\text{Collateral flow index, CFI} = \frac{P_{\text{occ}} - \text{CVP}}{P_{\text{ao}} - \text{CVP}}$$

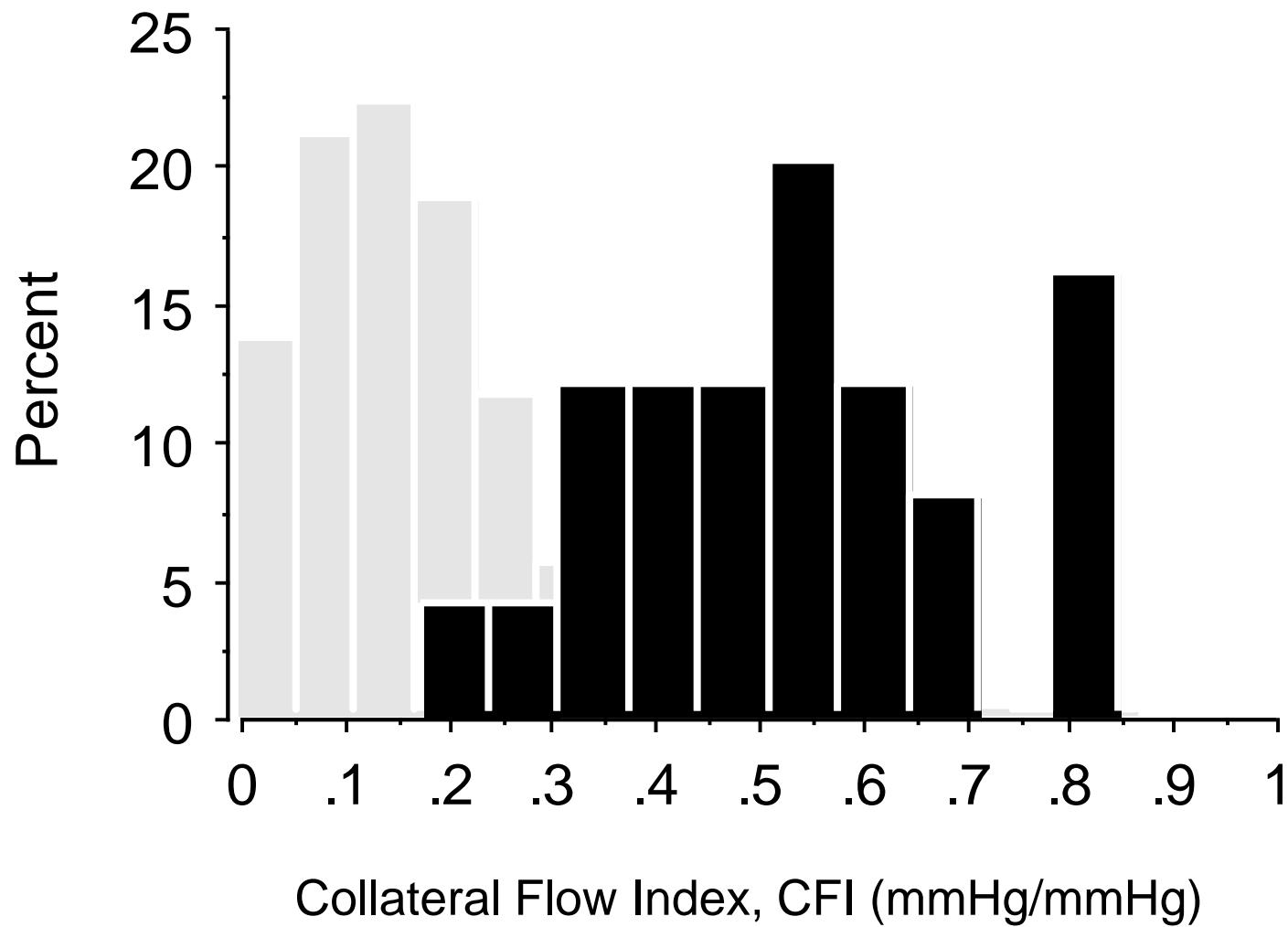
Traupe et al. Circulation 2010; 122: 1210-

Distribution of Human Coronary Collateral Function (n=1'740)

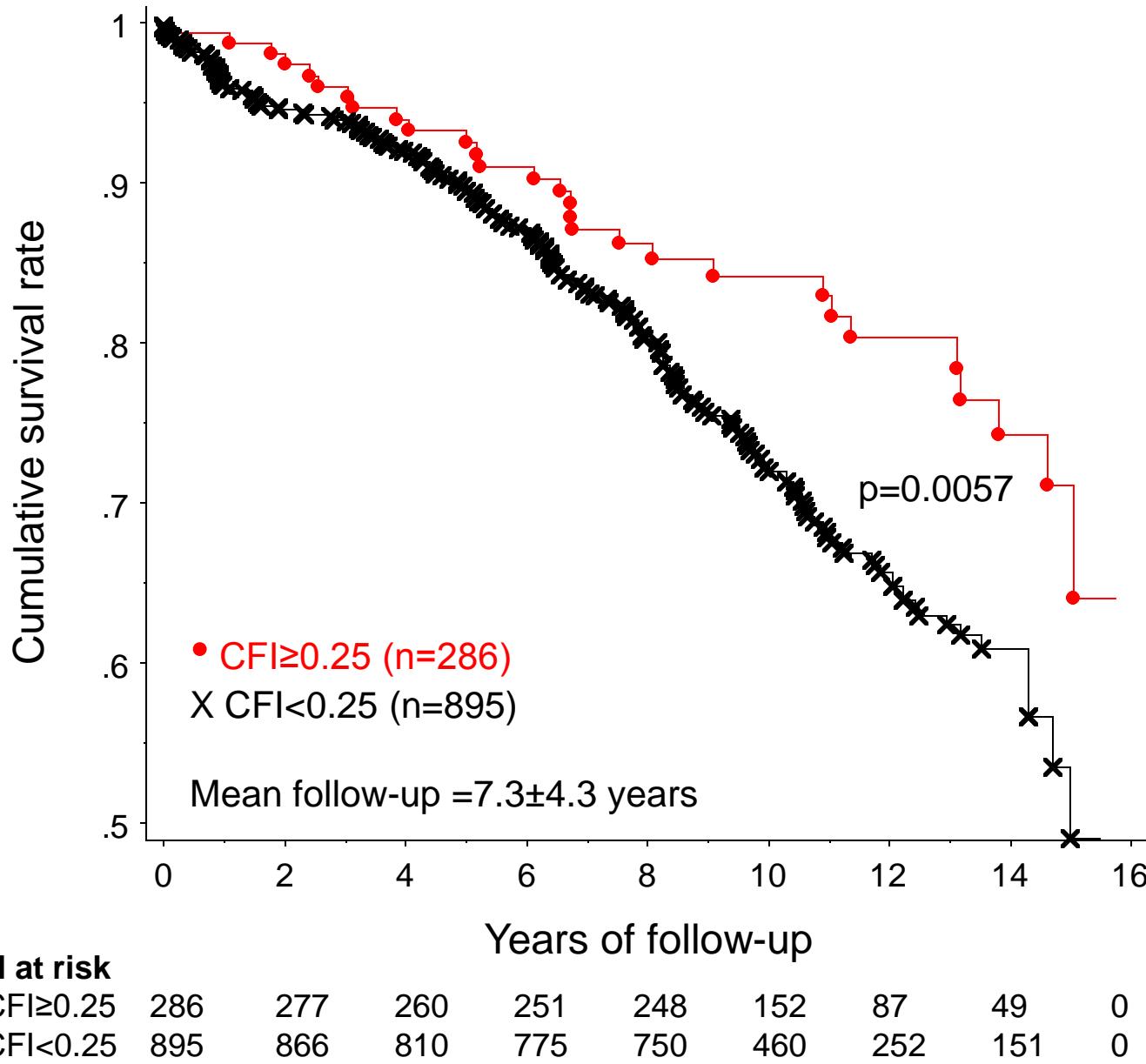




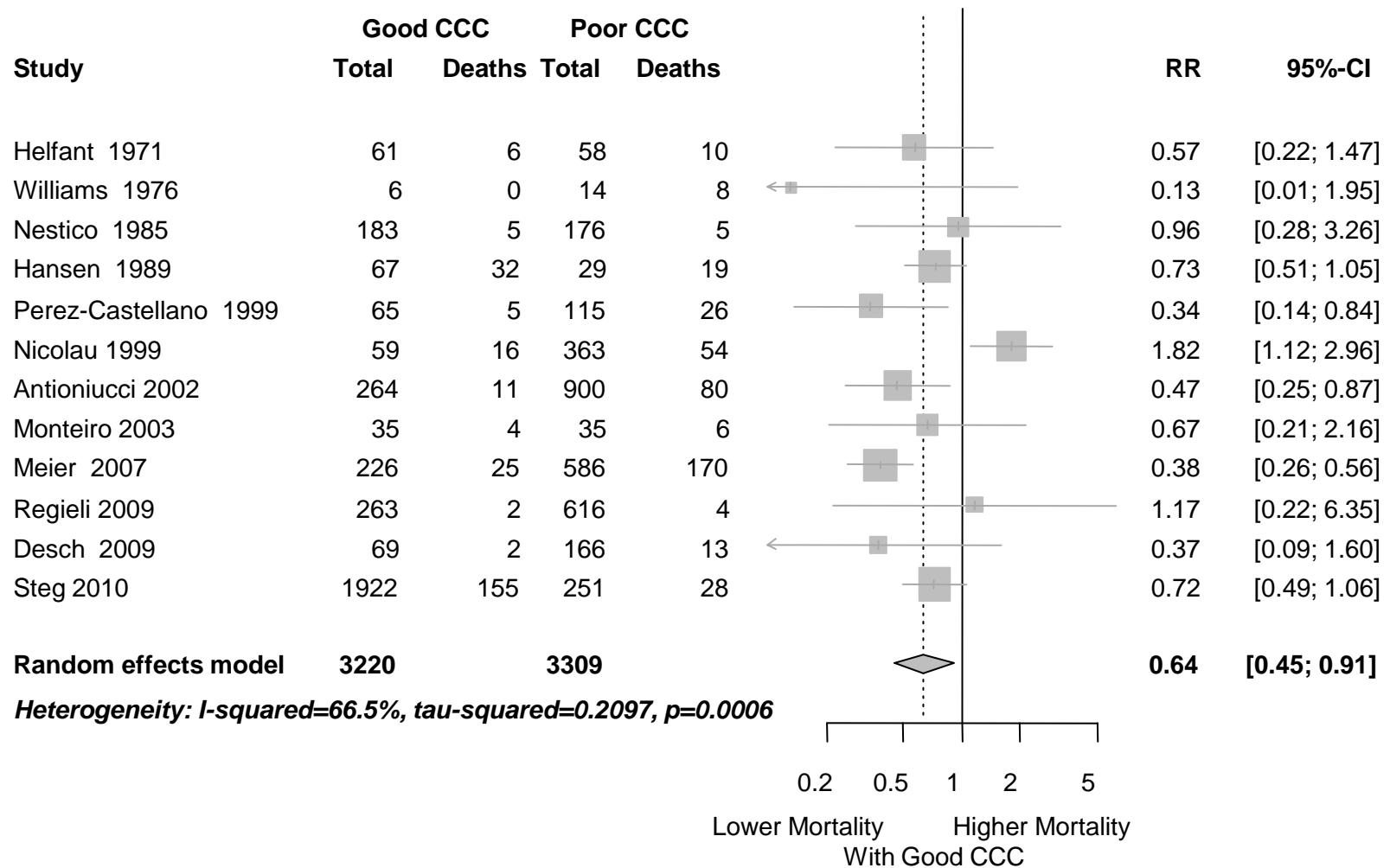
Coronary vs Peripheral (A. fem. s.) Circulation: Collateral Function



Collateral Flow Index (CFI) and All-Cause Mortality (n=234)

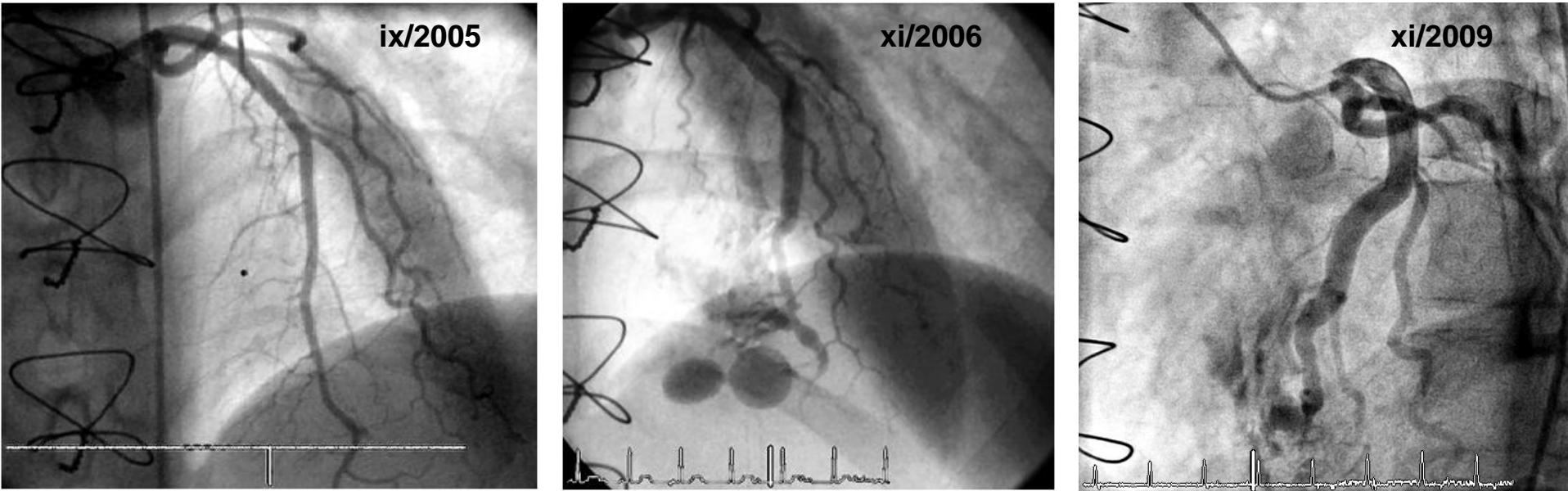


Impact of Coronary Collateral Circulation (CCC) on Survival

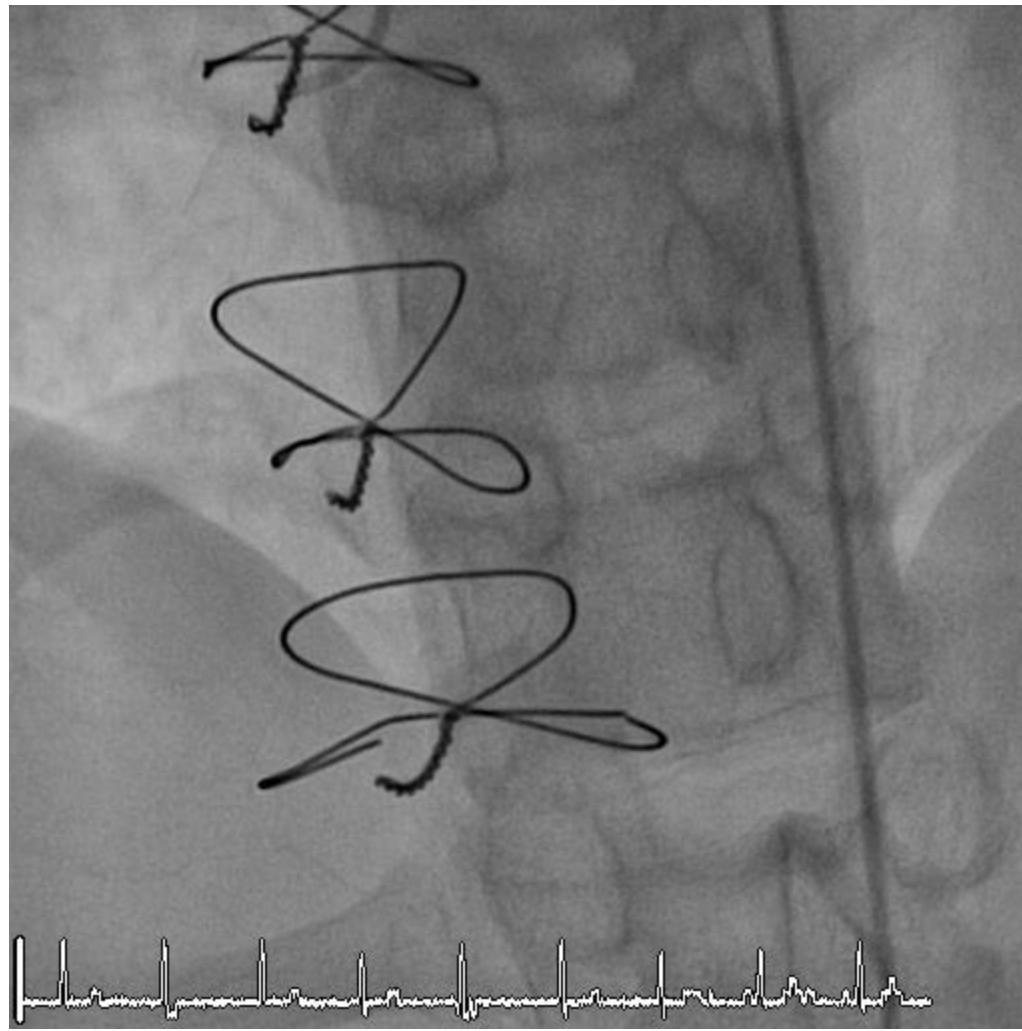


Meier P et al. Eur Heart J 2012; 33: 614-

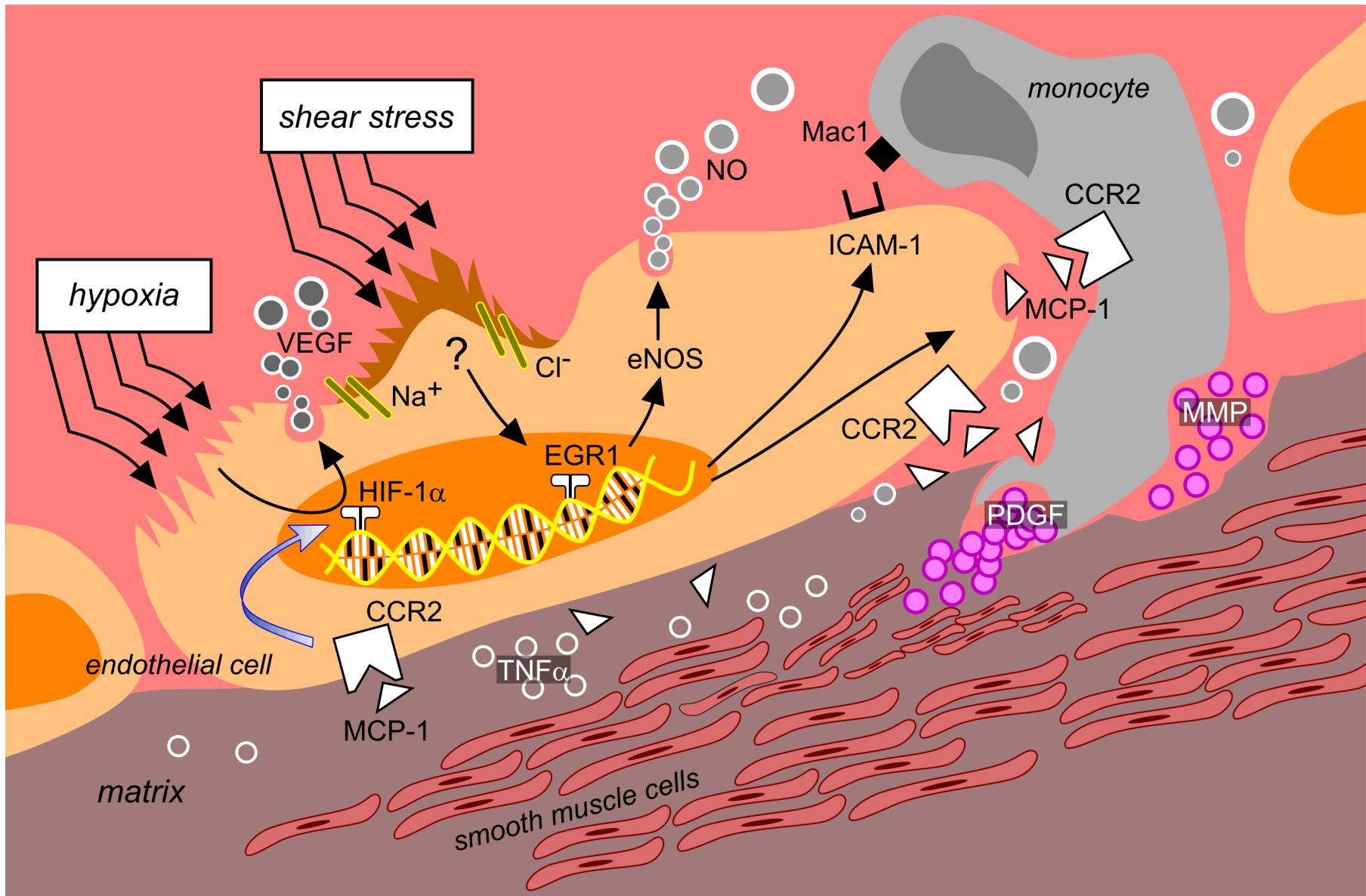
Physical Arteriogenesis



Vogel et al. Trends Cardiovasc Med 2010; 20: 129-

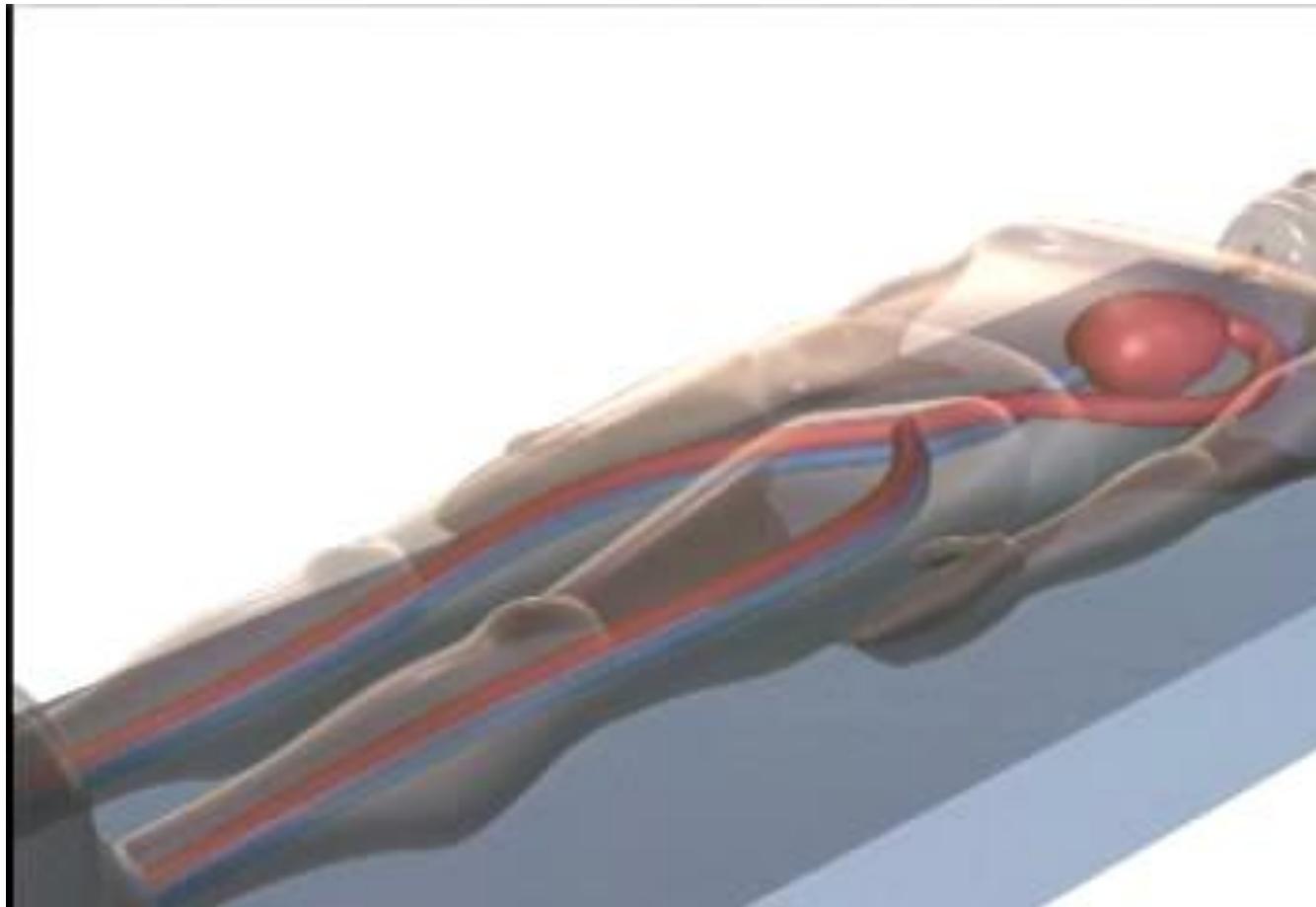


Molecular Pathways in Arteriogenesis

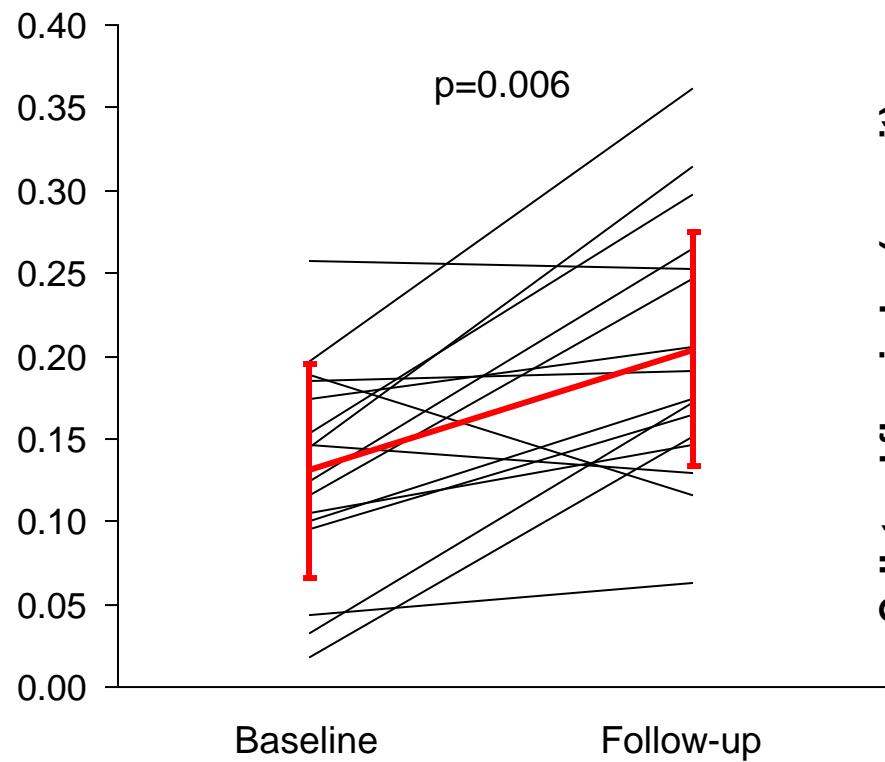


Seiler. Collateral Circulation of the Heart 2009; Springer

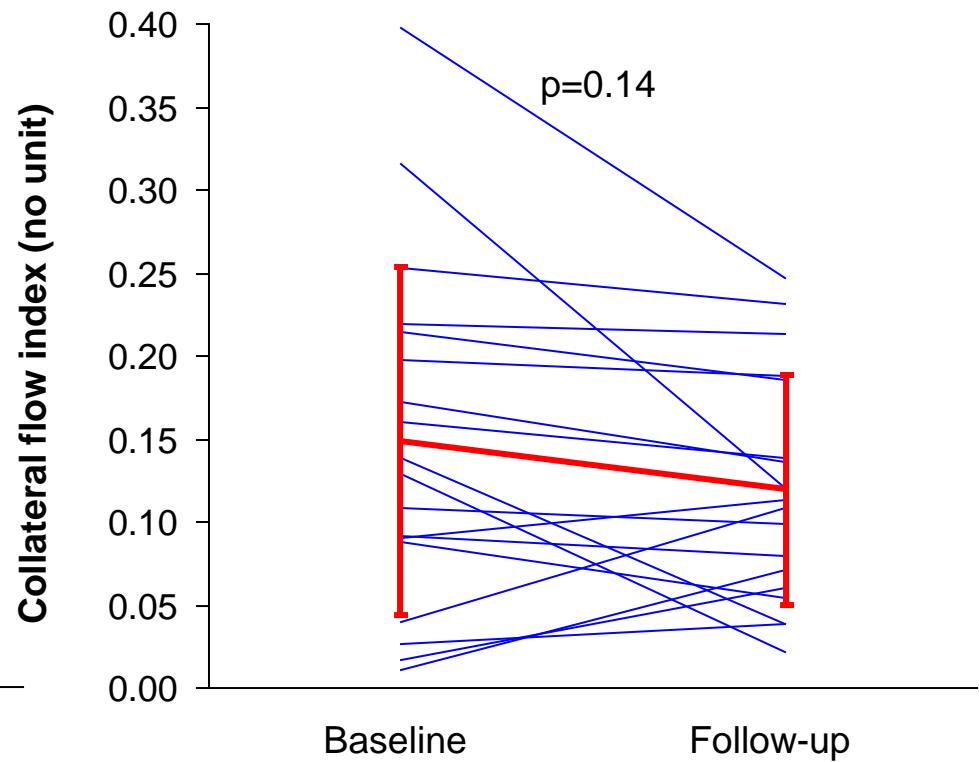
Increased Diastolic Coronary Shear Stress: External Counterpulsation (ECP)



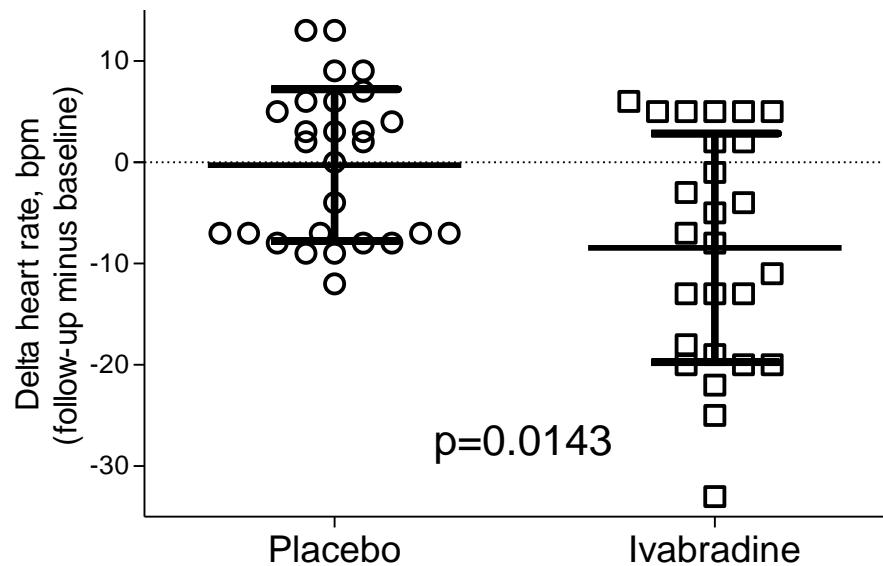
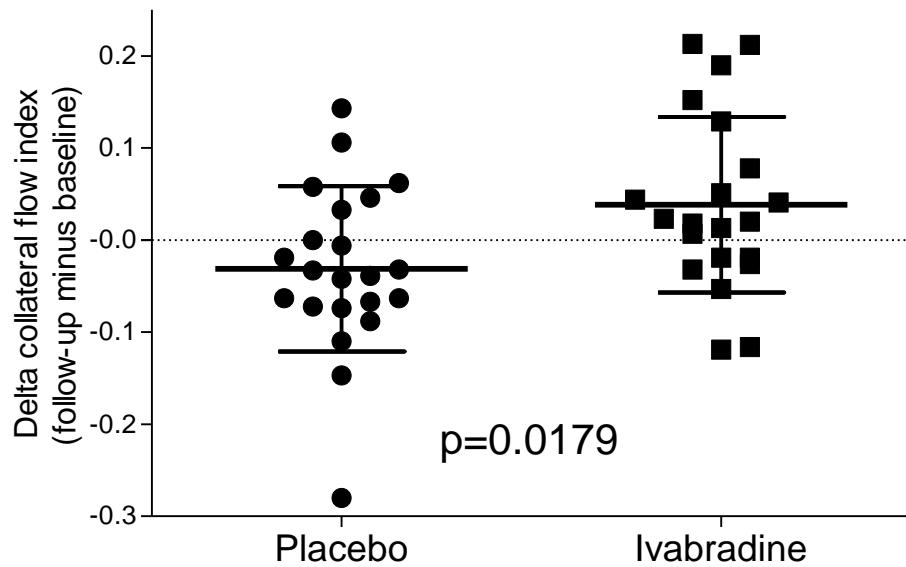
ECP

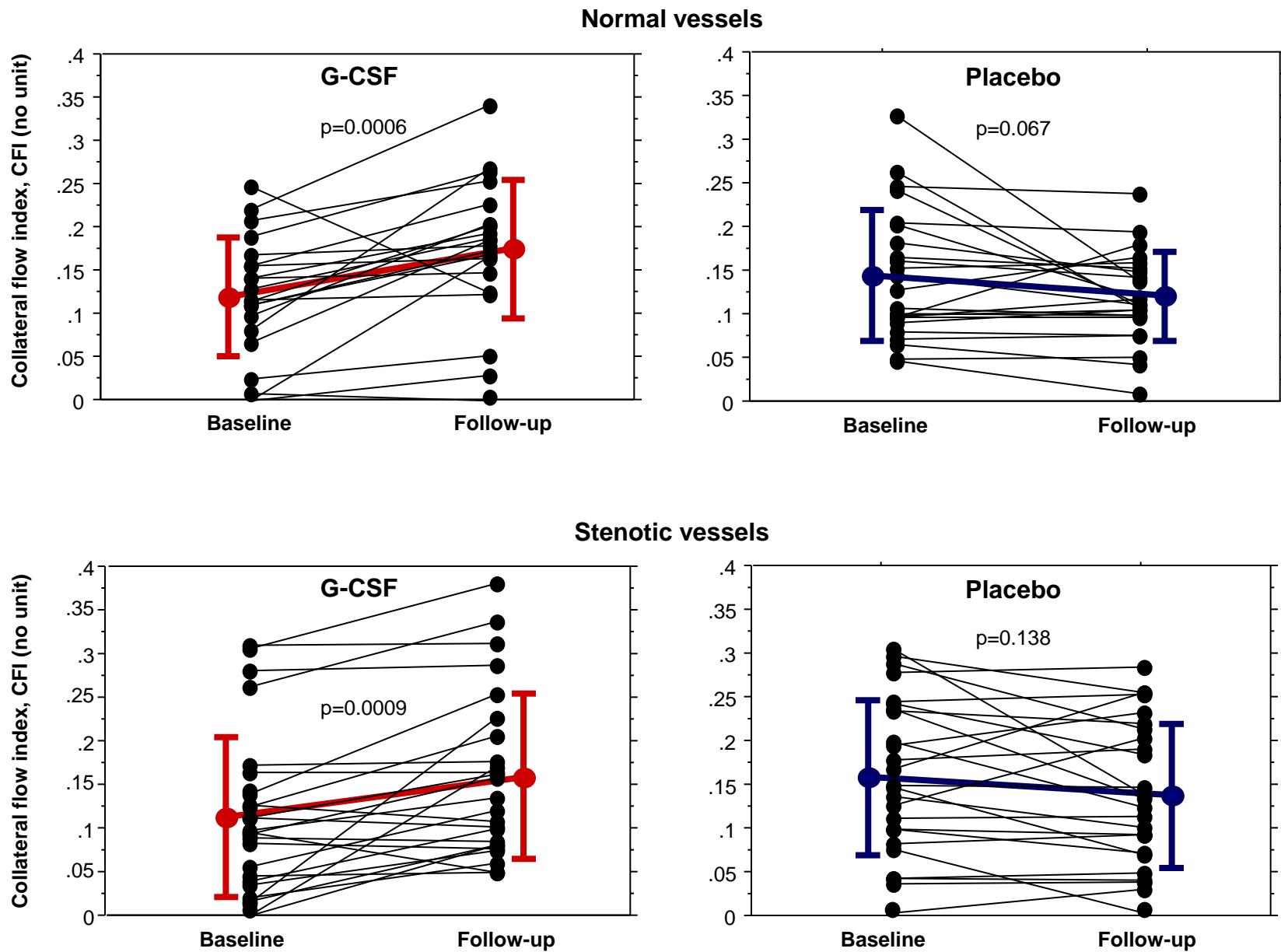


Sham ECP



Glöckler et al. Heart 2010; 96:202-



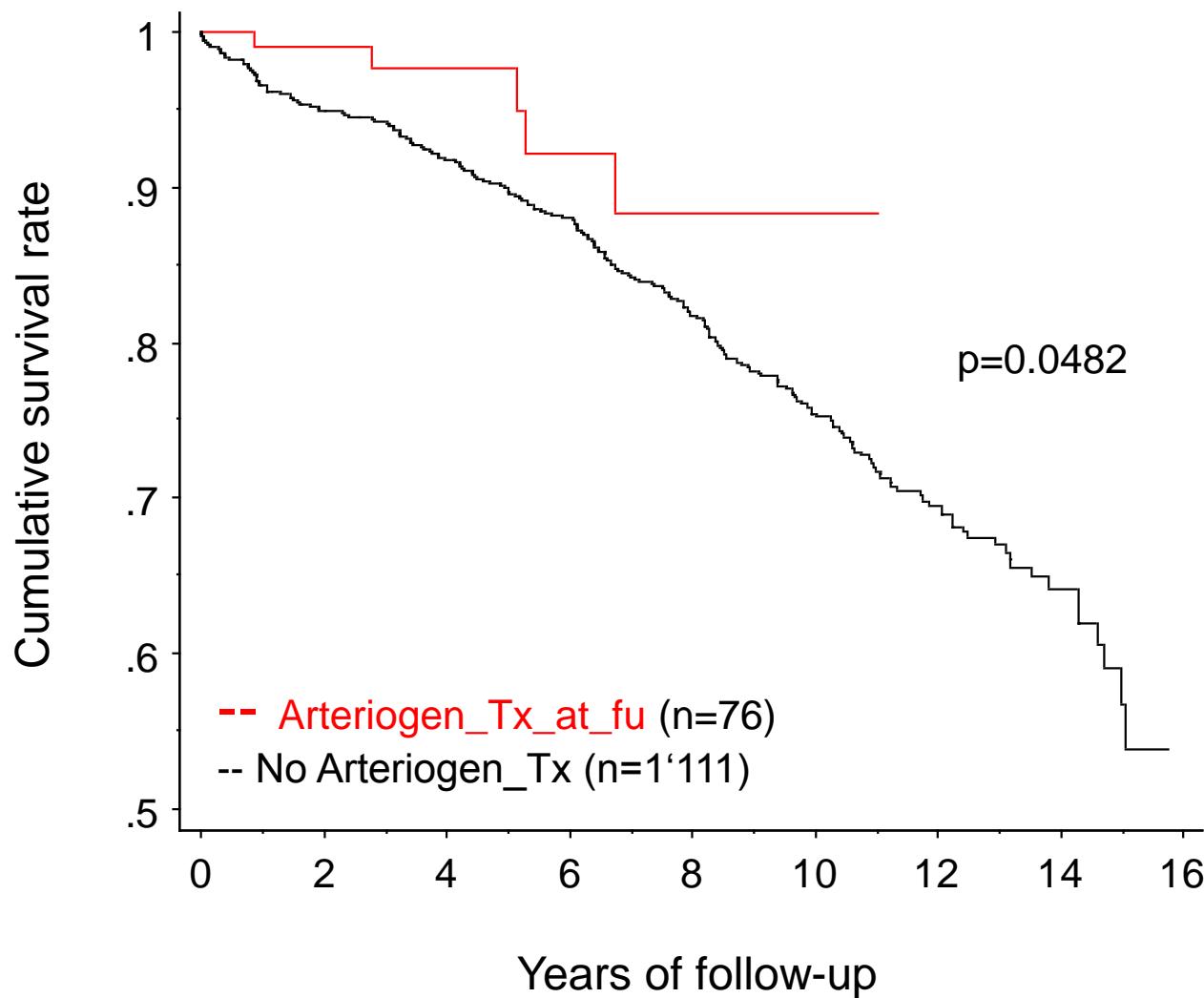


Protective Effect of Coronary Collaterals

- Sufficient CFI → ↓ infarct size
 - Sufficient CFI → ↓ mortality
 - Arteriogenic Tx → likely ↓ mortality
-
- Physical arteriogenesis:
 - ↑ diastolic flow velocity / duration
 - ECP, exercise, ivabradine
 - ECP: most significant ↑ collateral function

 - Chemical arteriogenesis:
 - Monocyte activation by growth factors
 - Granulocyte colony stimulating factors
 - MCP-1 (cave: atherogenesis)

Arteriogenic Therapy and All-Cause Mortality (n=234)

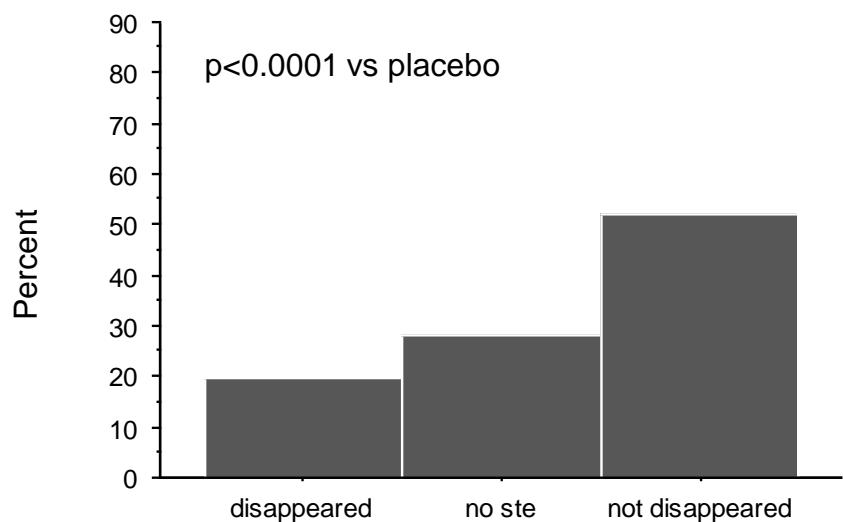


N at risk

Arteriogen_Tx	76	54	33	18	15	9	0	0	0
No Arteriogen_Tx	1'111	1'070	1'009	956	931	580	313	190	0

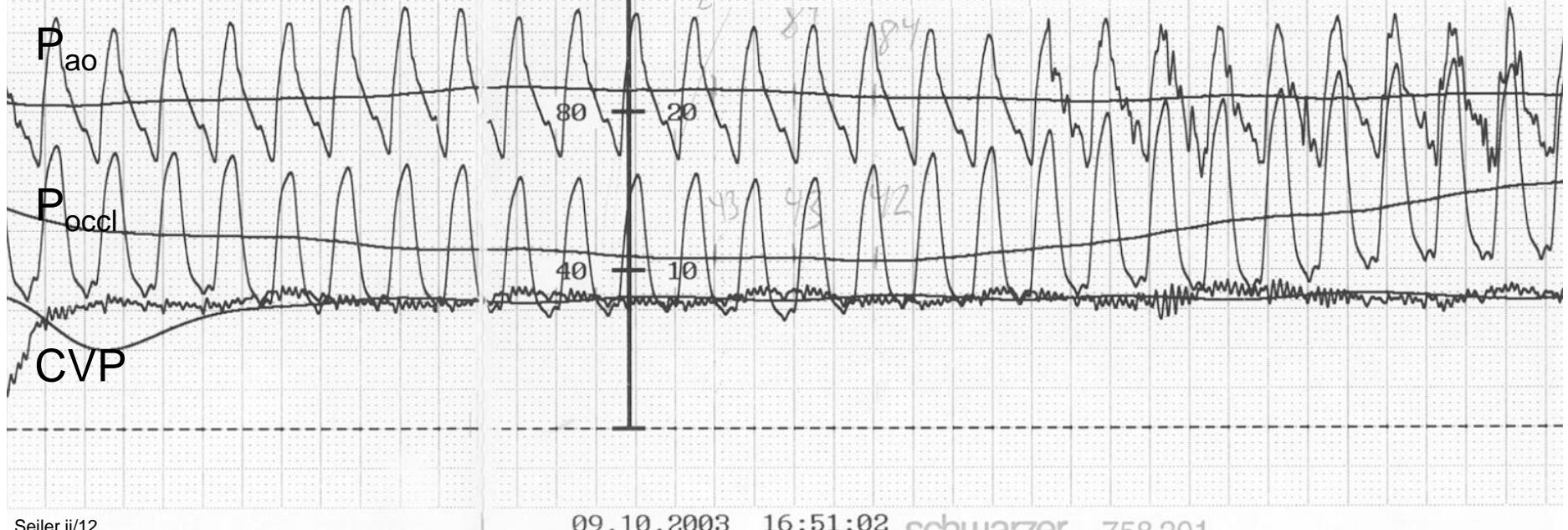
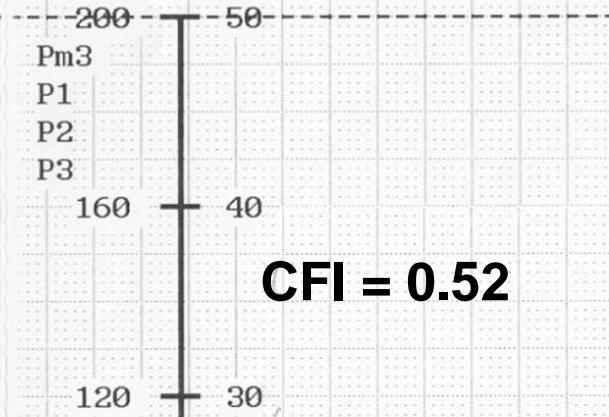
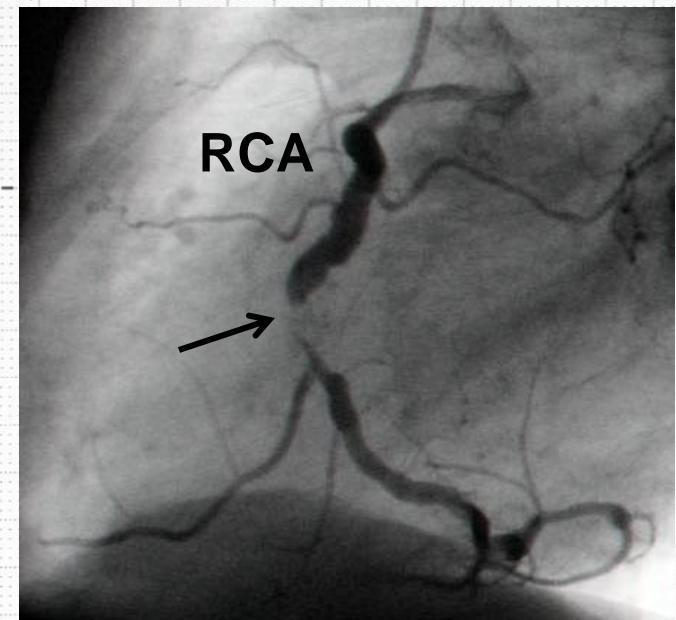
Arteriogenesis by Granulocyte-Colony Stimulating Factor (G-CSF)

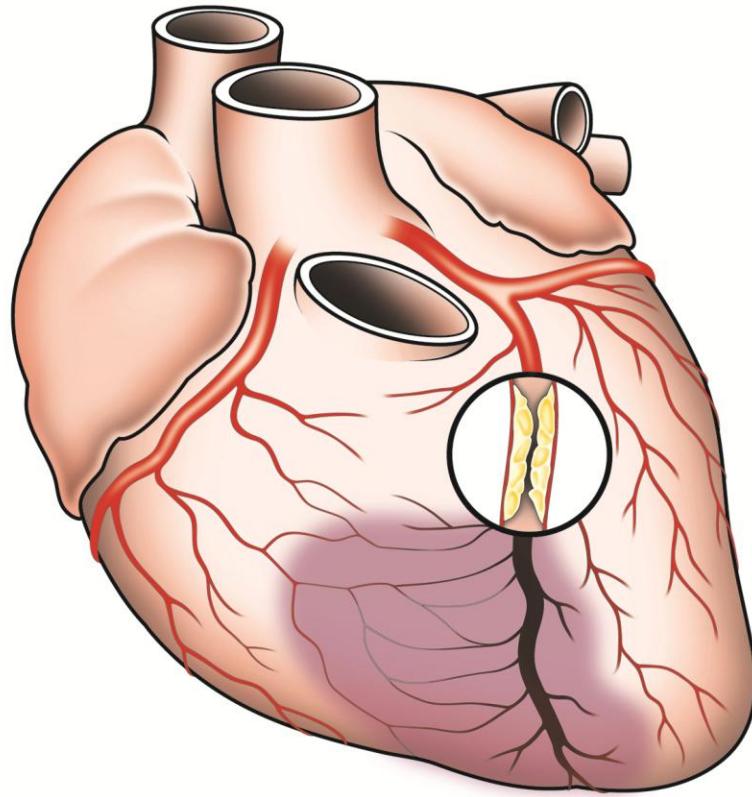
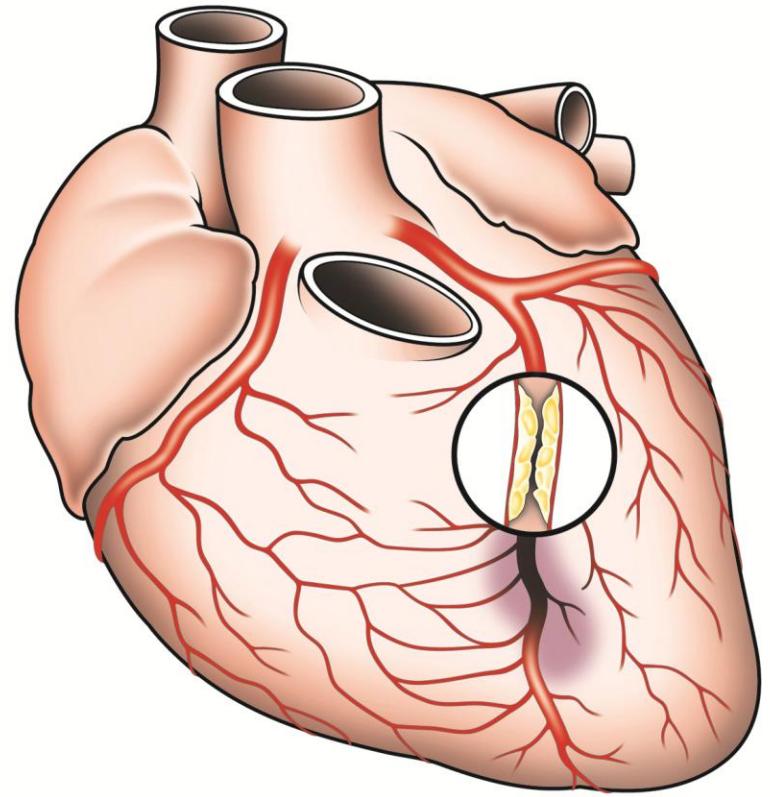
G-CSF (n=26)



Placebo (n=26)

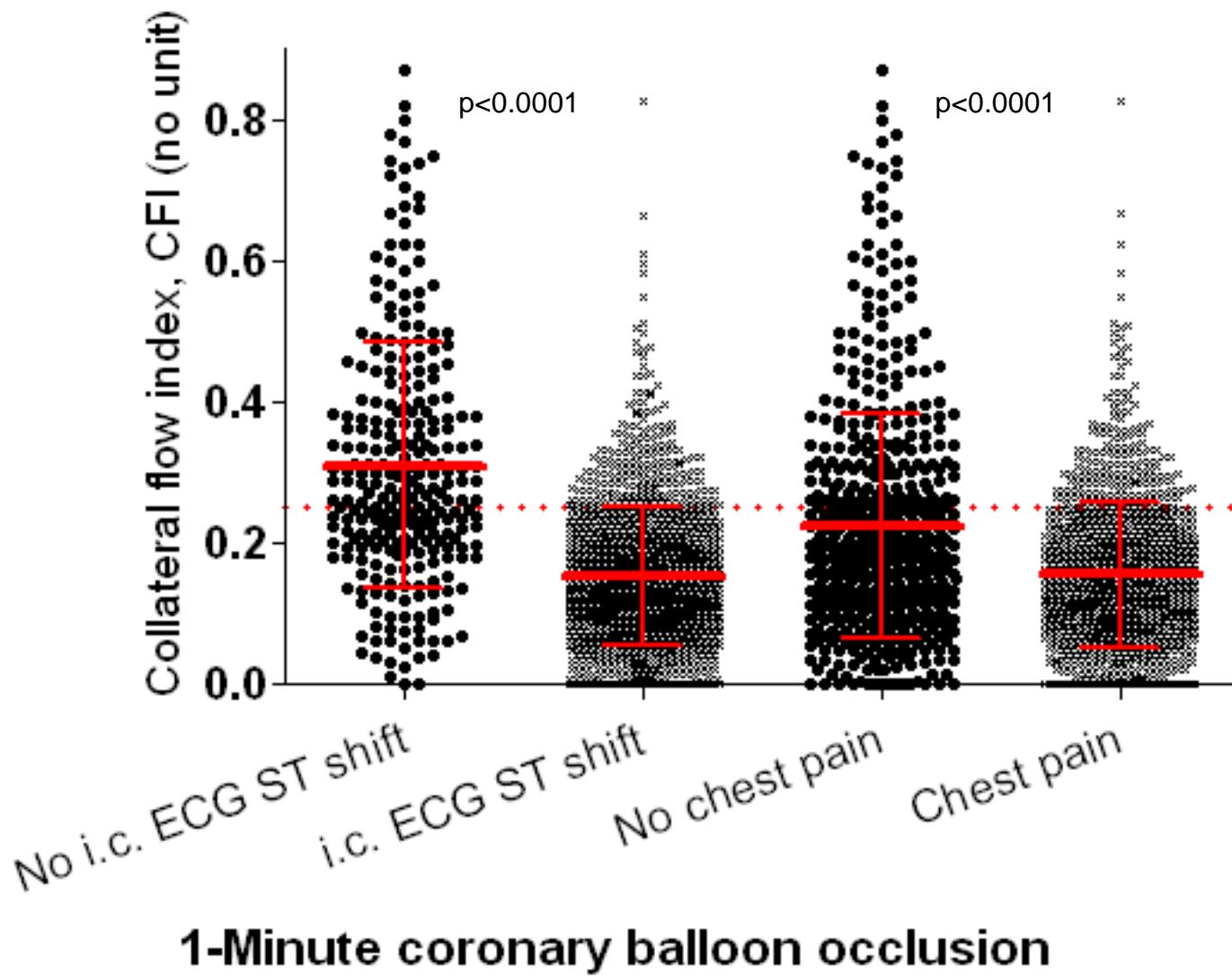




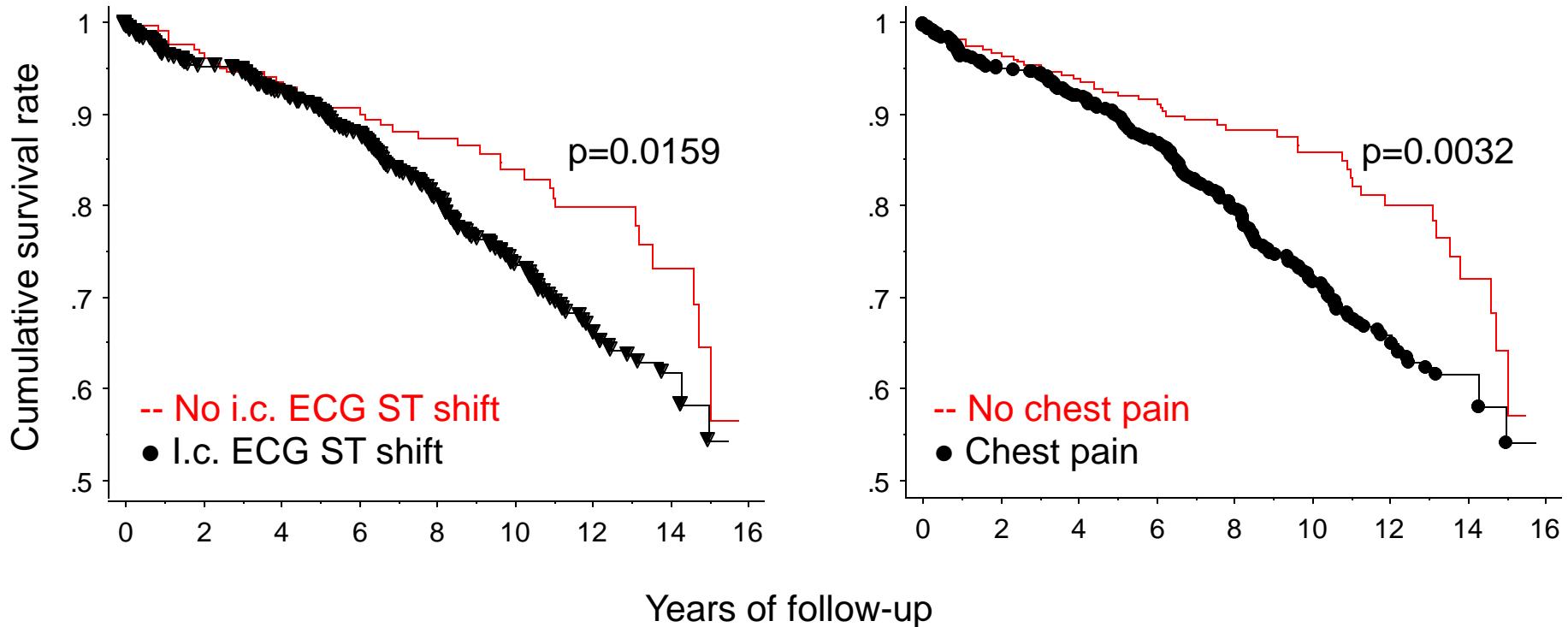


Meier P and Seiler C. Heart 2013; epub ahead of print

1-min Coronary Occlusion: Signs of Ischemia and CFI (n=1'740)



Ischemia During Coronary Occlusion and All-Cause Mortality (n=234)

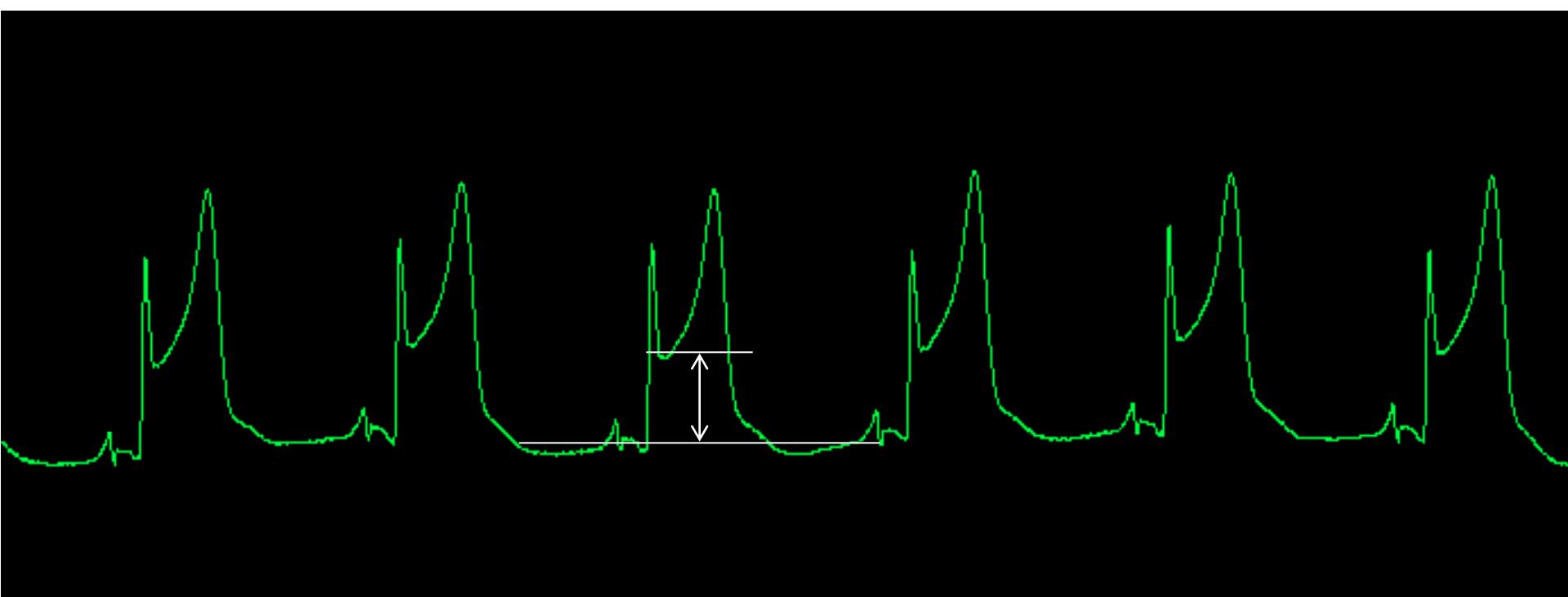


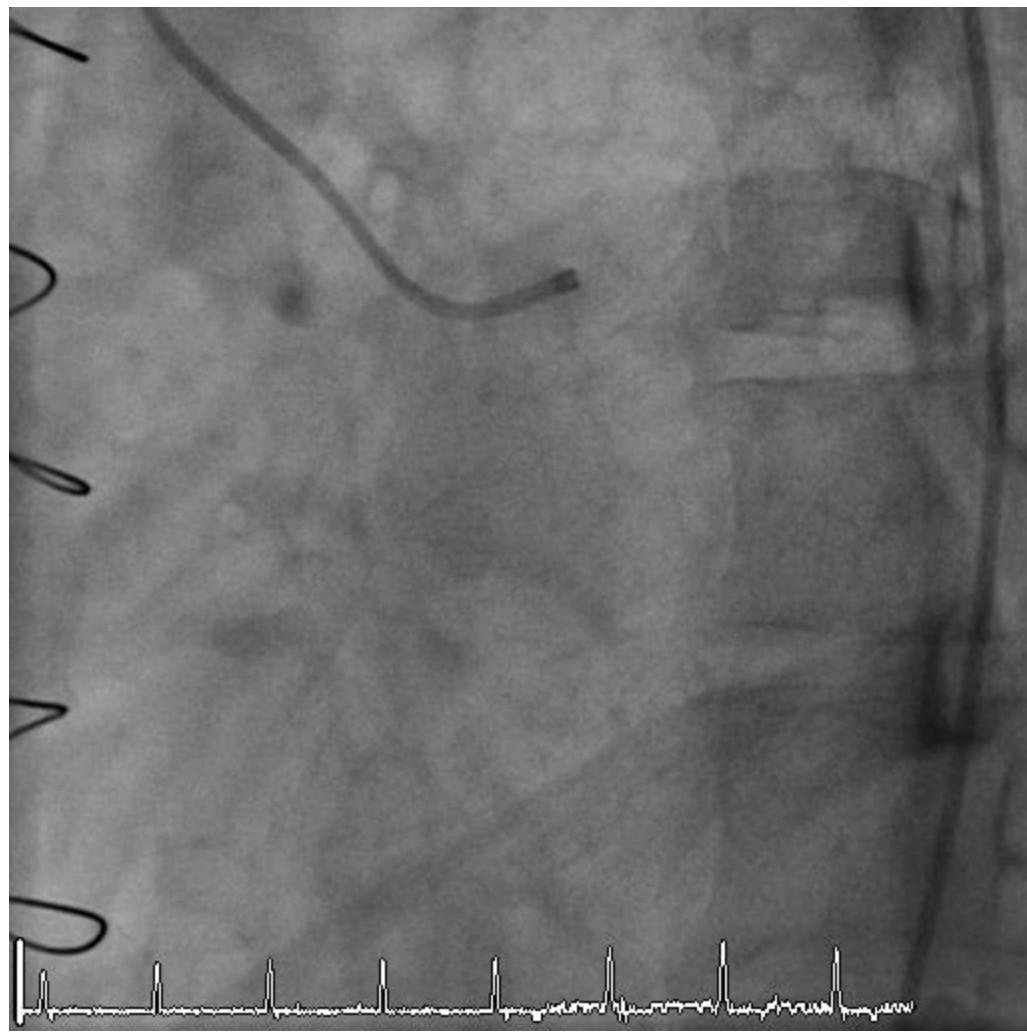
N at risk

No ST shift	286	231	202	59	201
ST shift	895	763	702		

No chest pain	286	235	211	81	0
Chest pain	895	794	694	235	0

Intracoronary ECG During Coronary Occlusion



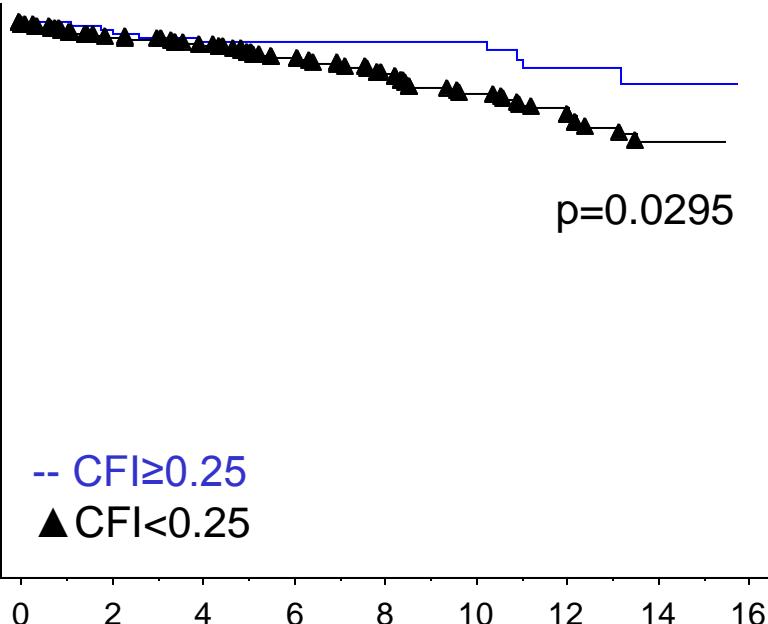


Cumulative event-free survival rate

Cardiac Deaths (n=90)

 $p=0.0295$

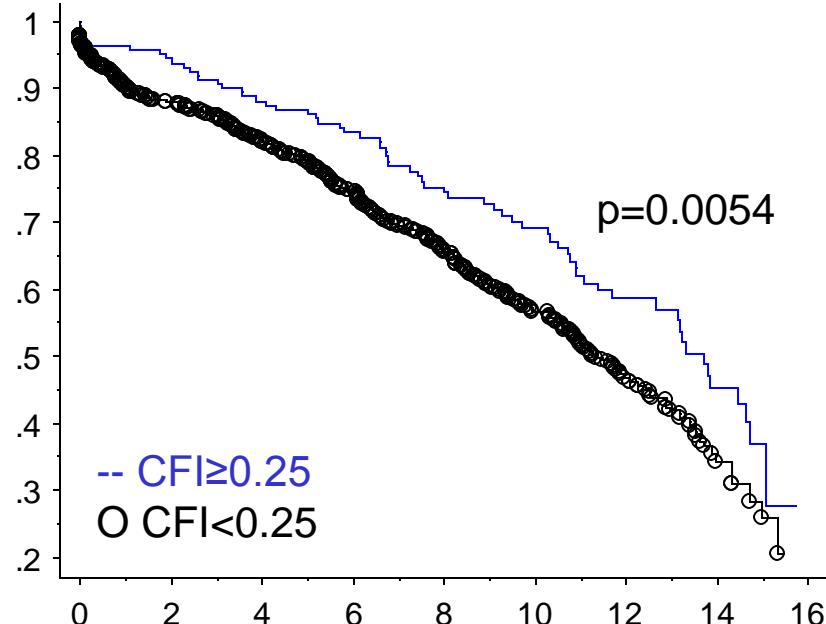
-- CFI ≥ 0.25
 ▲ CFI < 0.25



Major Adverse Cardiac Events (n=442)

 $p=0.0054$

-- CFI ≥ 0.25
 O CFI < 0.25



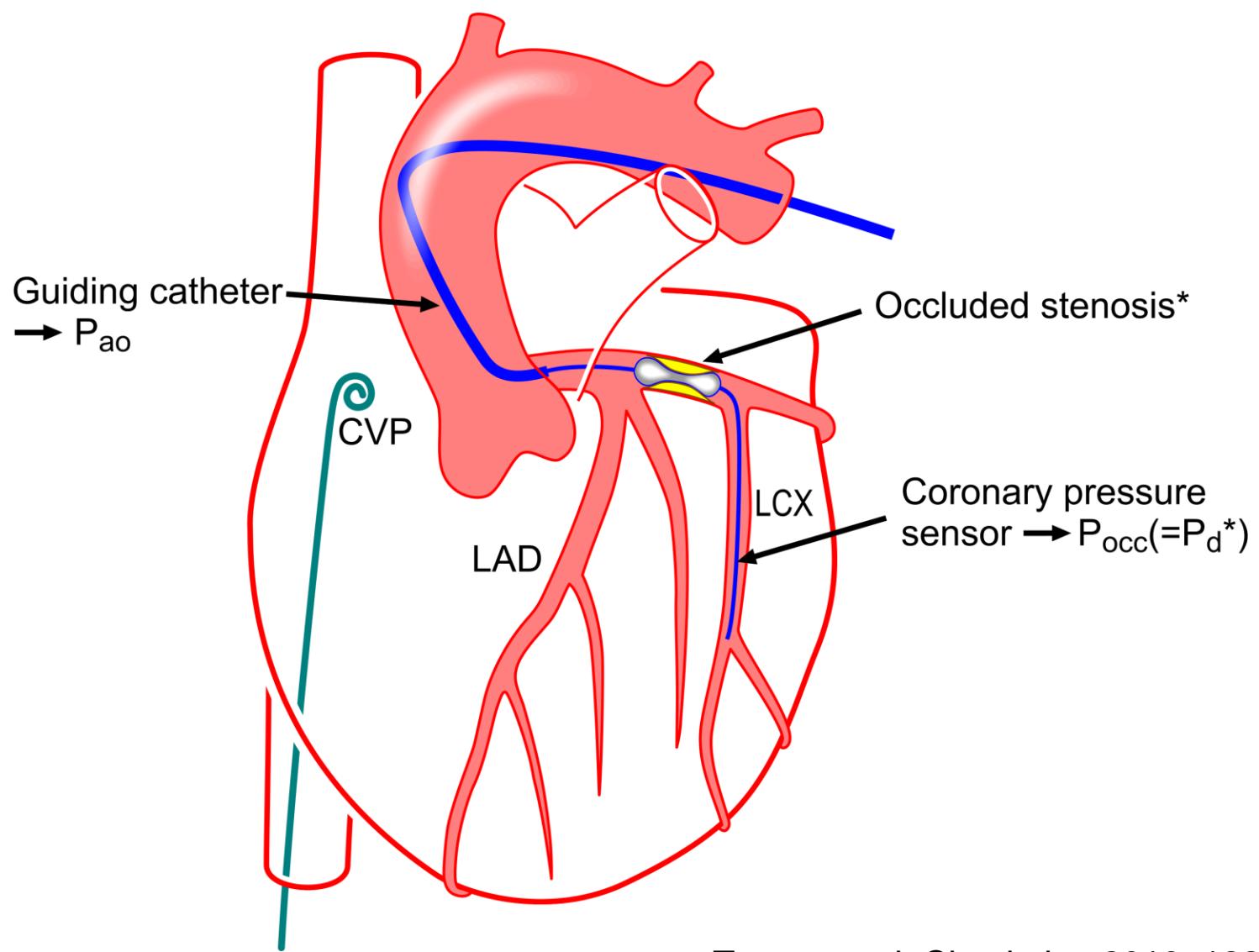
Years of follow-up

N at risk

CFI ≥ 0.25	286	248	222	88	0	286	237	201	76	0
CFI < 0.25	895	780	760	250	0	895	702	603	243	0

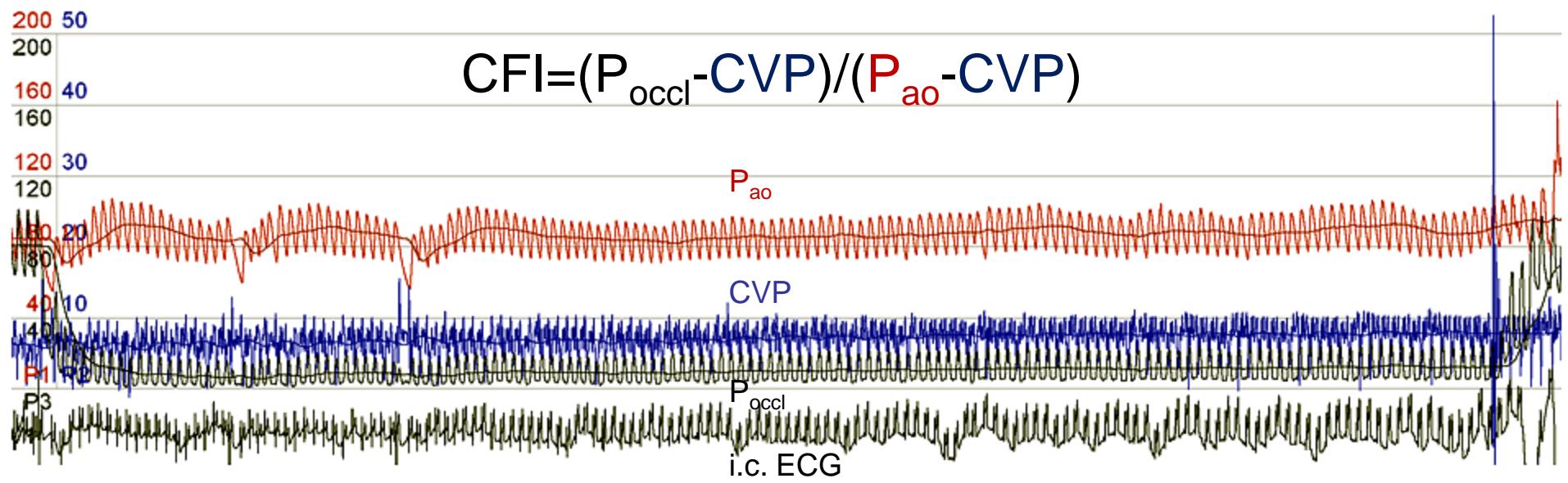
Figure 4

Coronary Pressure-Derived Collateral Flow Index (CFI)

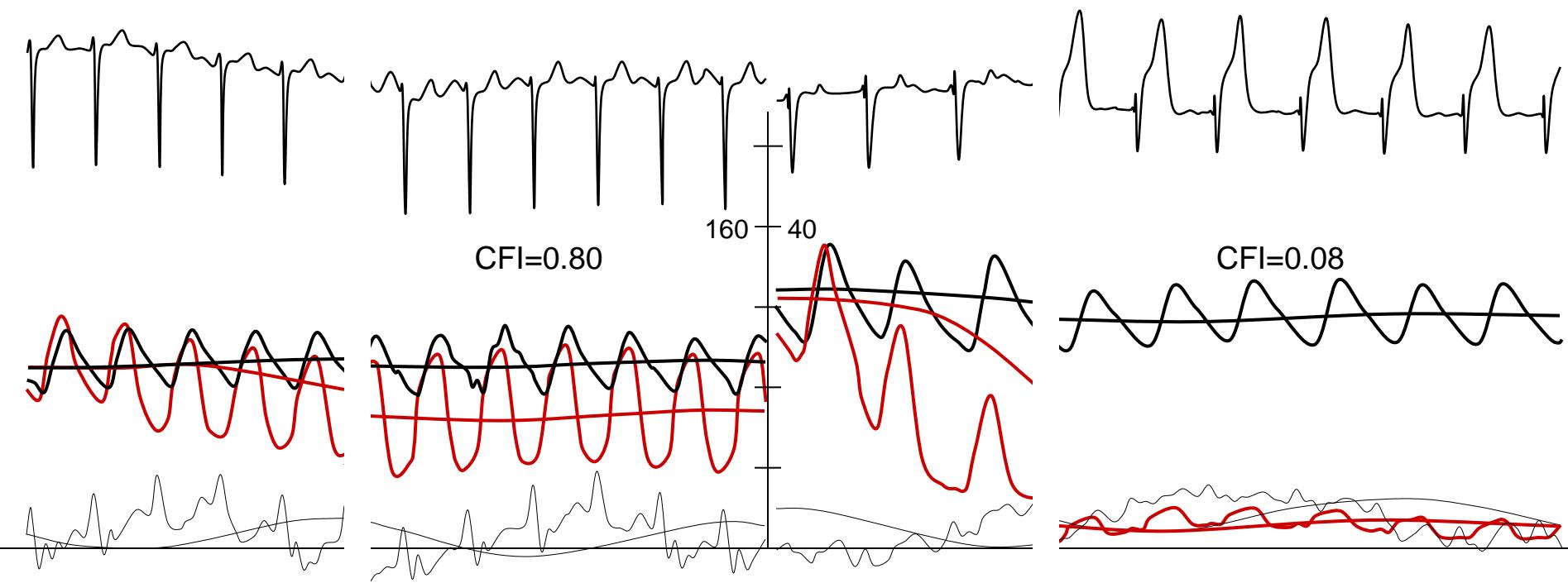


Traupe et al. Circulation 2010; 122: 1210-

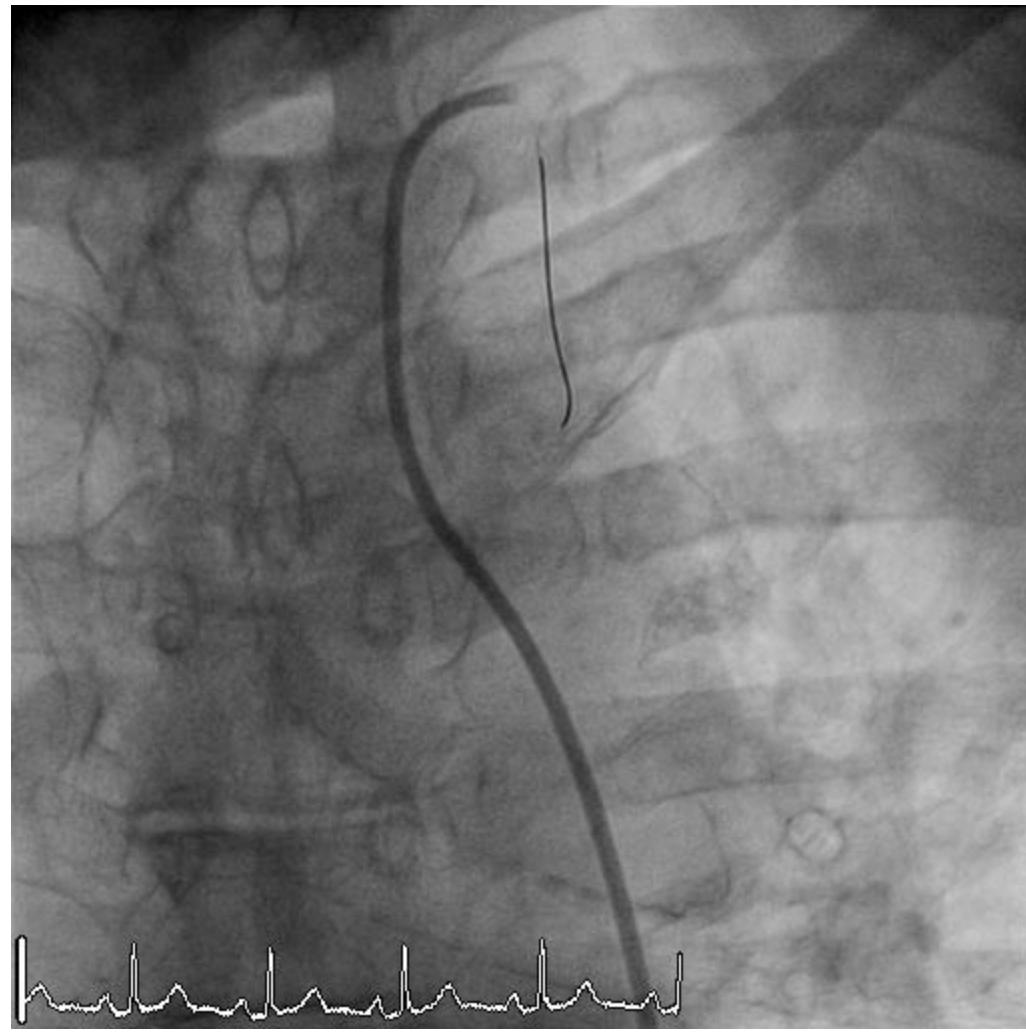
← 2 minutes →



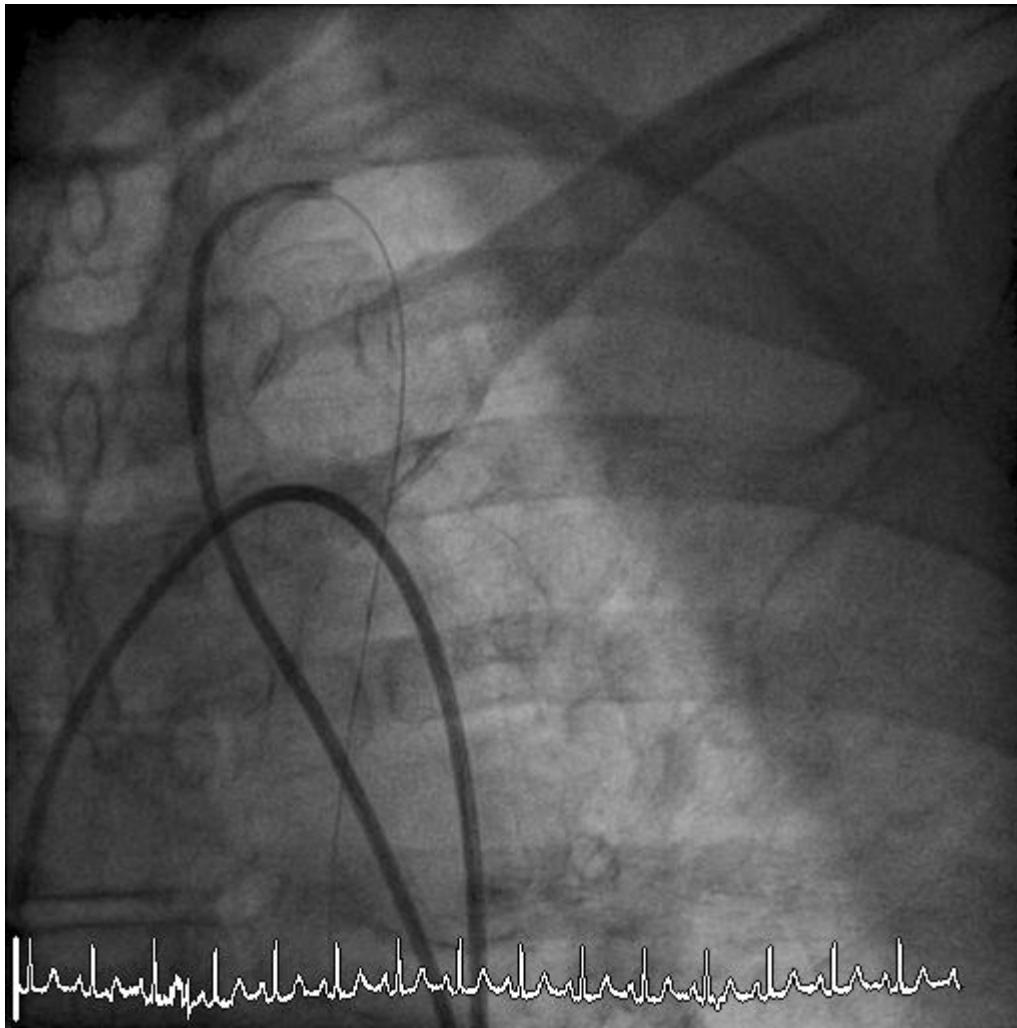
Coronary Pressure-Derived Collateral Flow Index (CFI)



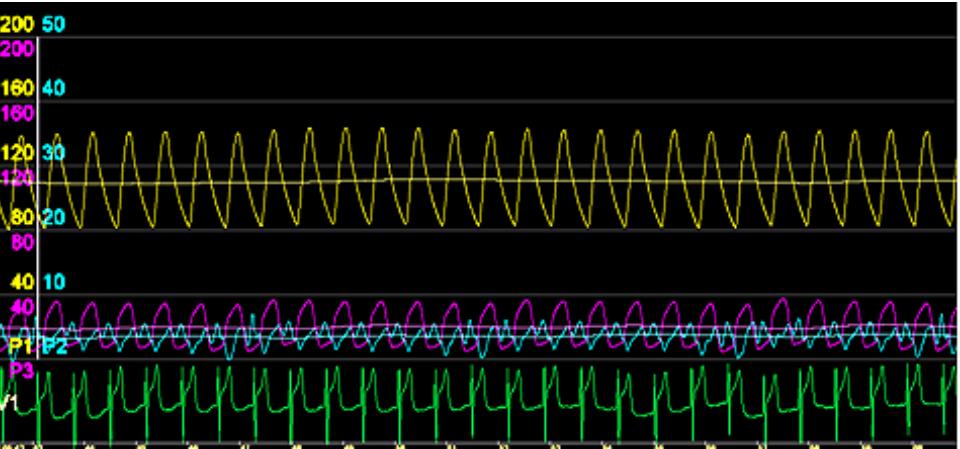
Traupe et al. Circulation 2010; 122: 1210-



Extracardiac Coronary Collateral Supply by the IMA(s) ?

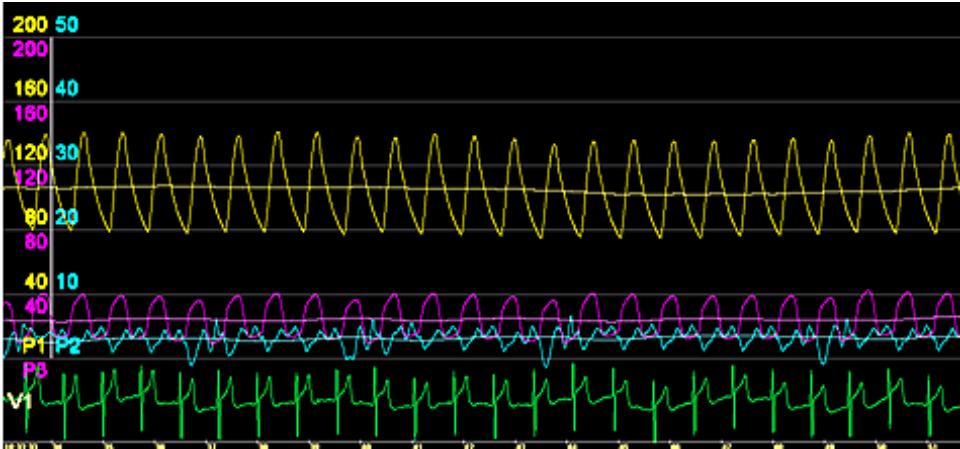


CFI without LIMA-Occlusion



CFI = 0.138

CFI with LIMA-Occlusion



CFI = 0.195

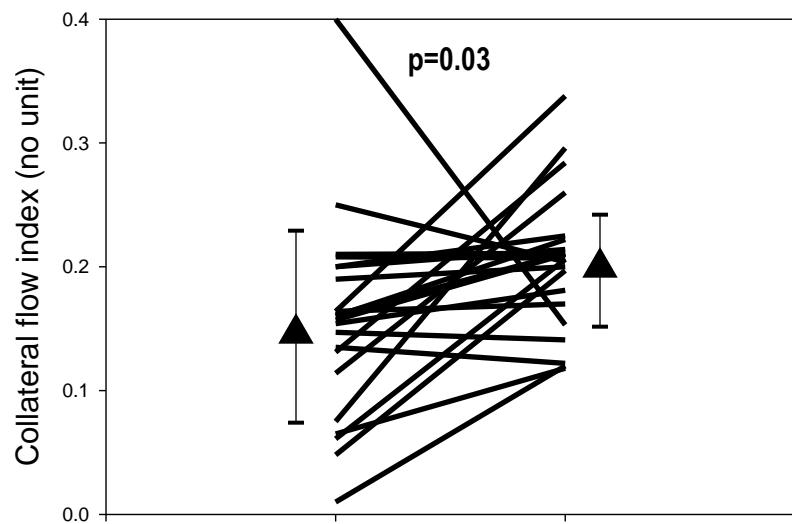


#11 / 12.03.12

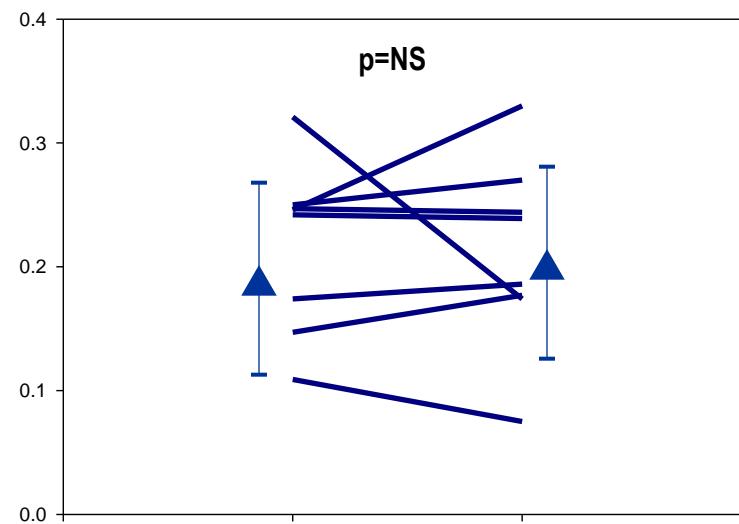
„Wer seine Kollateralen trainiert, lebt länger. Eindrucksvoll haben das der Arzt ..., von der Universitätsklinik für Kardiologie und Kollegen in Bern nachgewiesen, als sie die Daten von 6‘529 Patienten auswerteten: ..“

von Jörg Blech

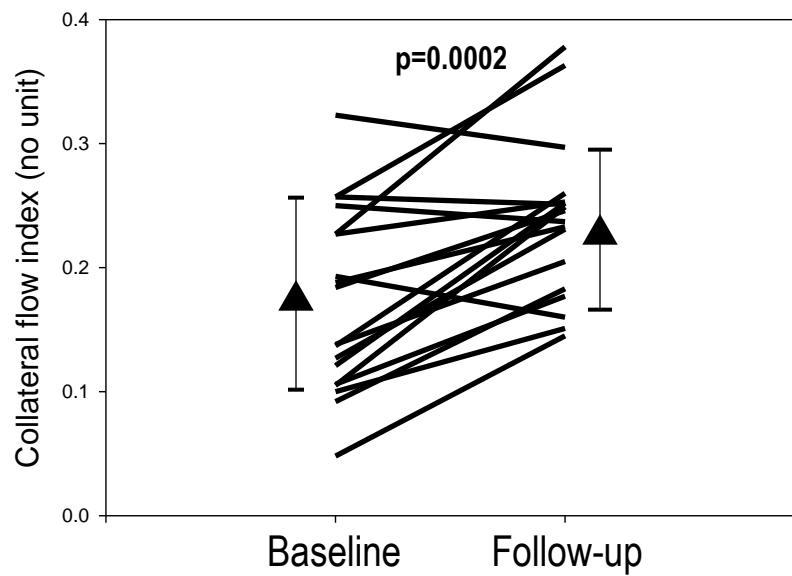
Stenotic Artery, Exercise Group



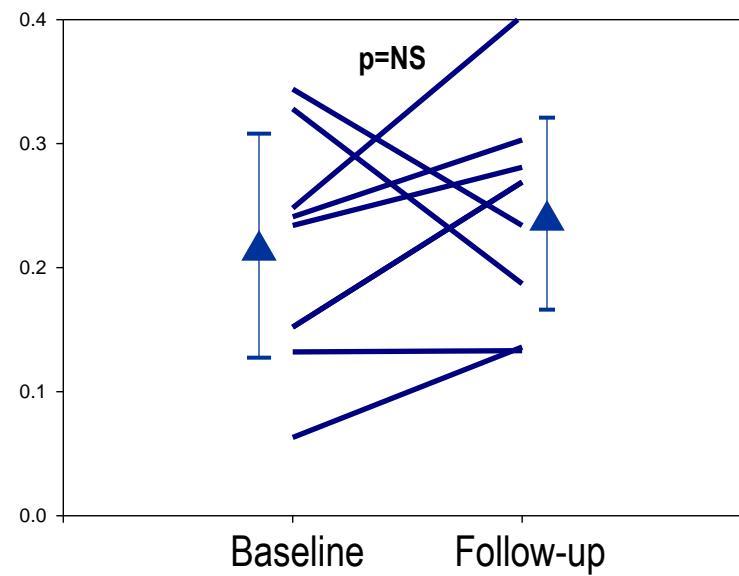
Stenotic Artery, Sedentary Group



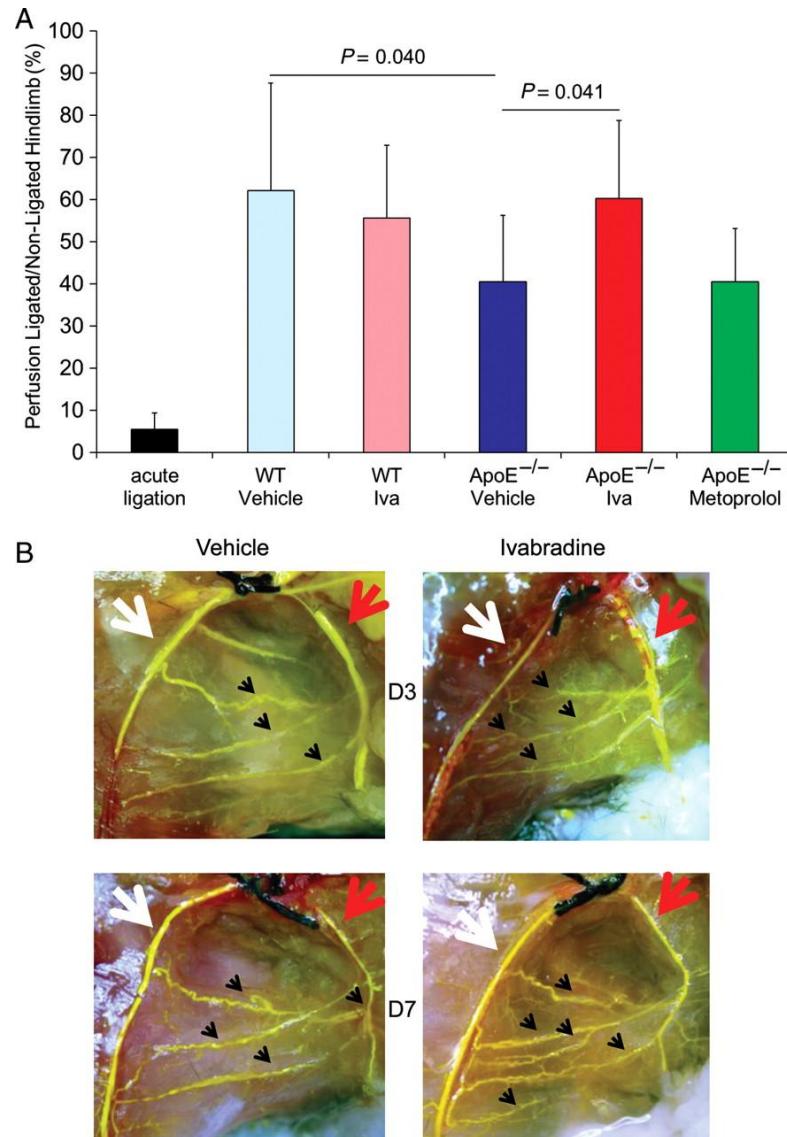
Normal Artery, Exercise Group



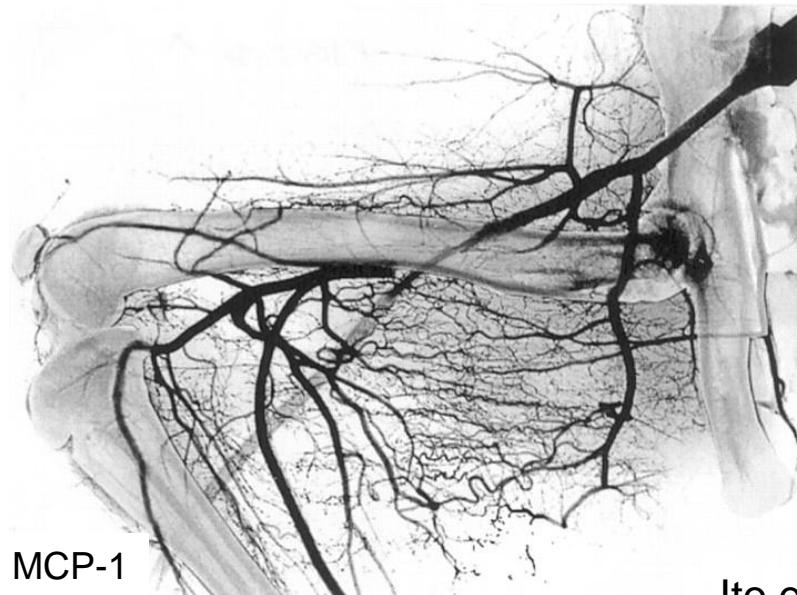
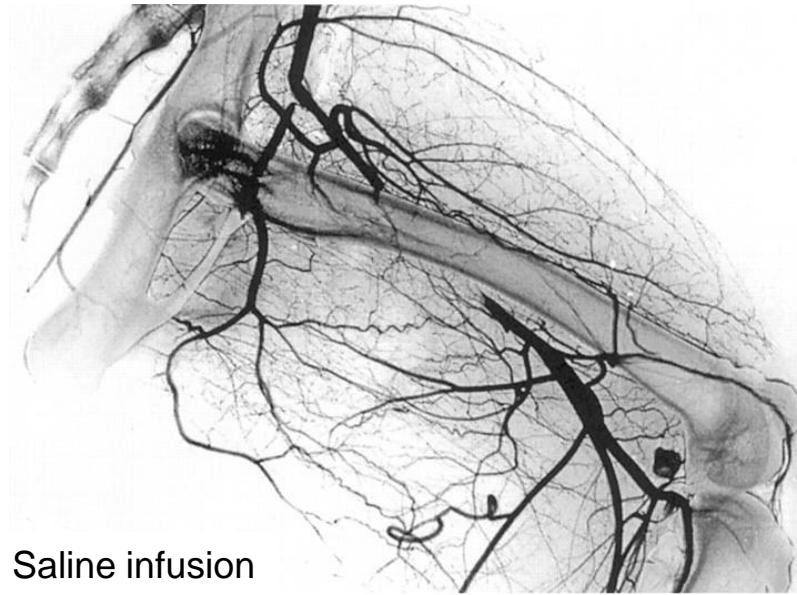
Normal Artery, Sedentary Group



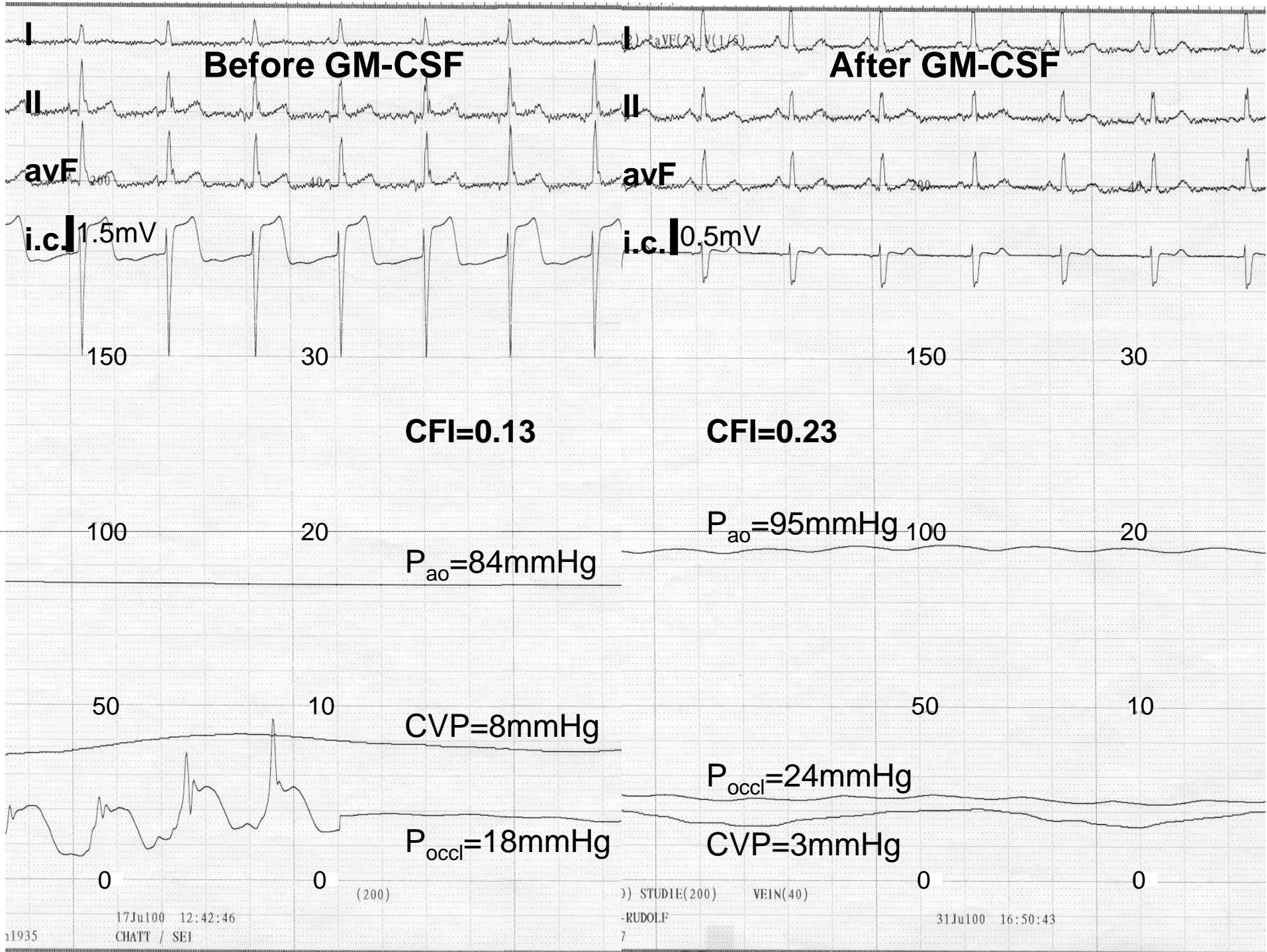
Hindlimb Arteriogenesis in Apo-E^{-/-} Mice by Ivabradine



Hindlimb Arteriogenesis in Rabbits by Monocyte Chemotactic Protein-1

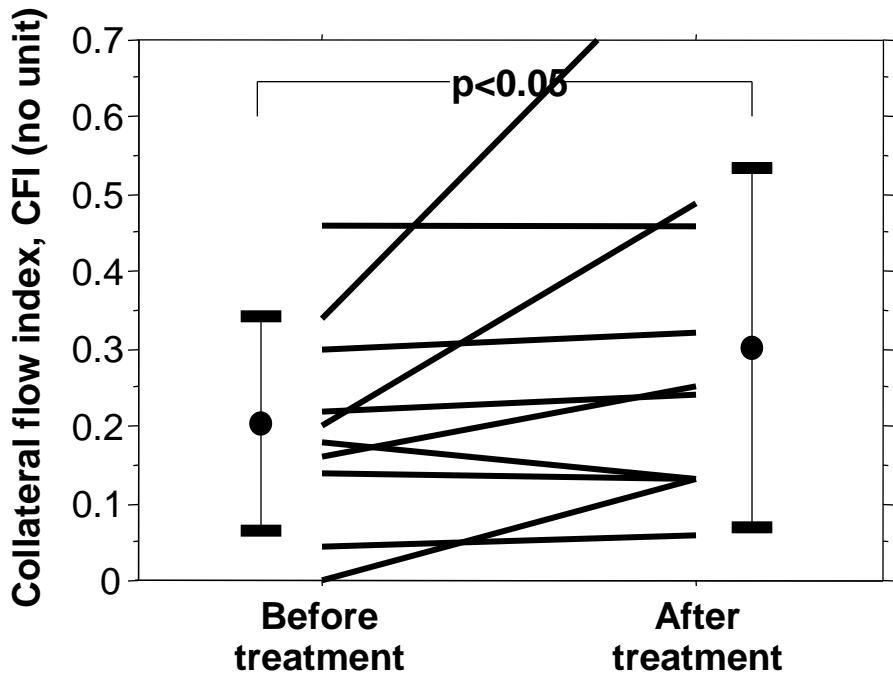


Ito et al. Circ Res 1997; 80: 829-

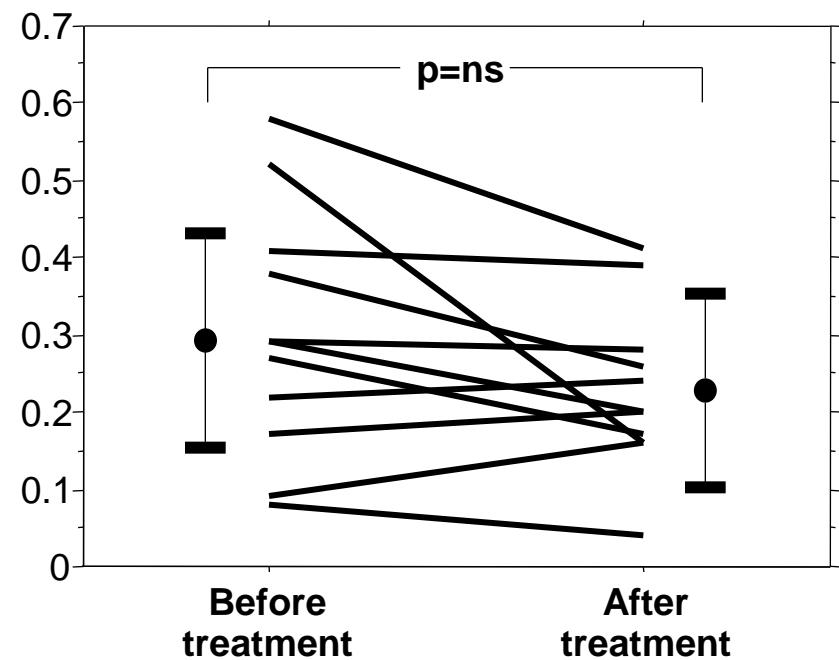


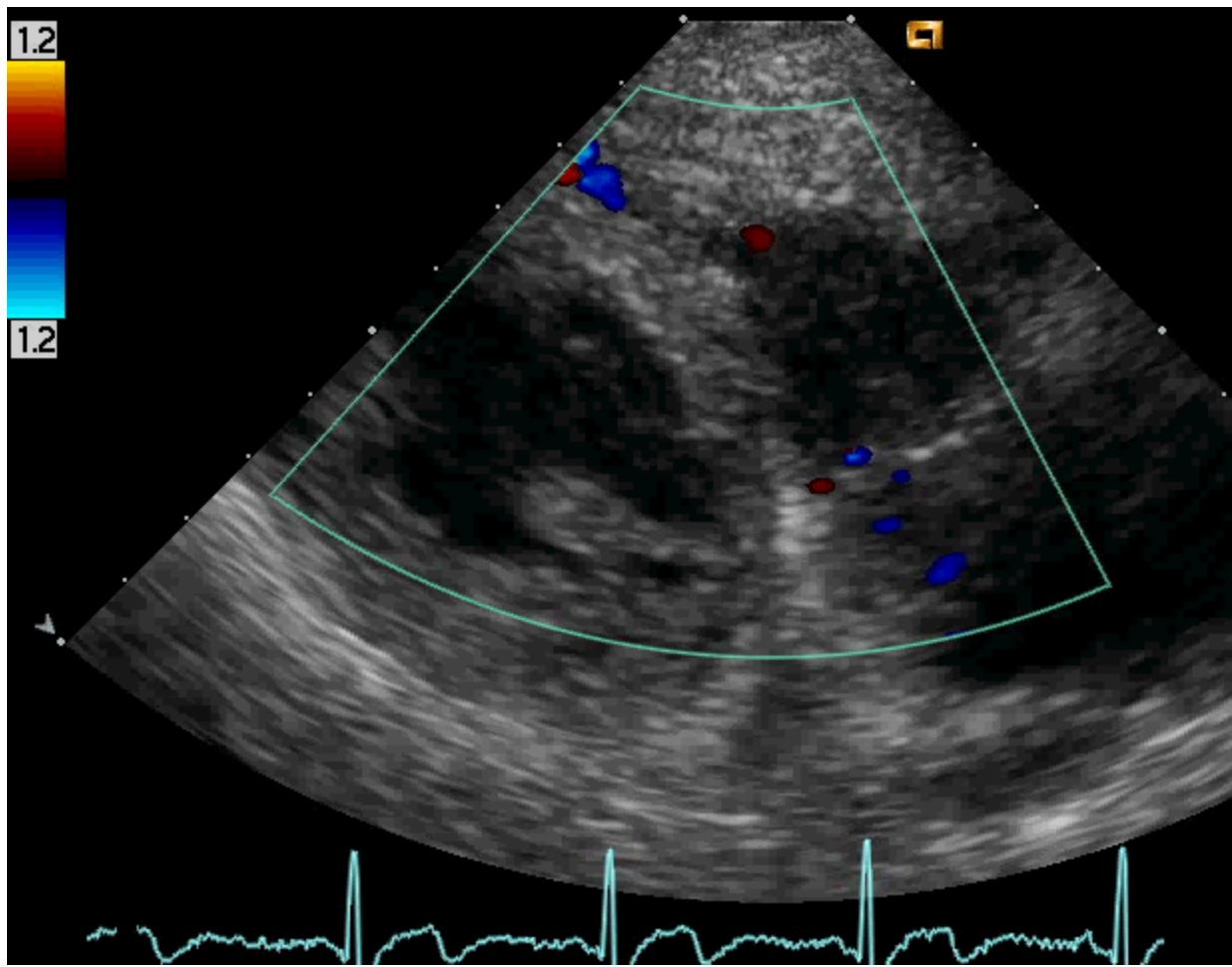
Arteriogenesis by Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF)

GM-CSF

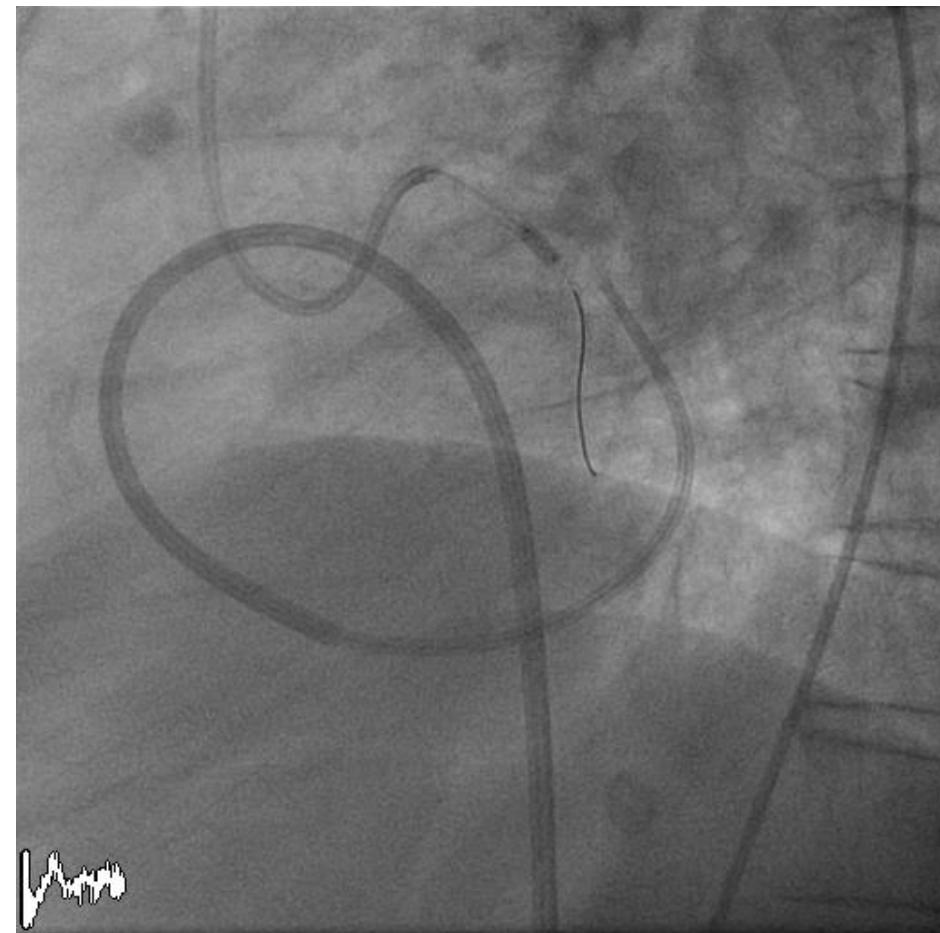
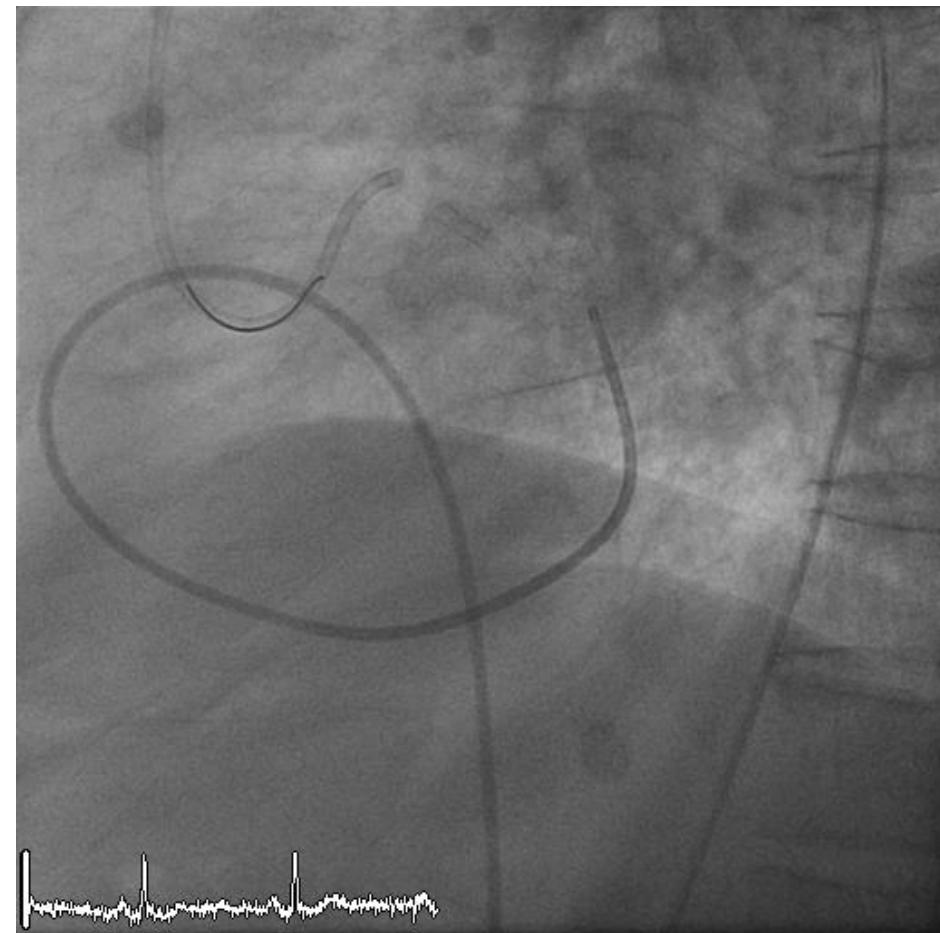


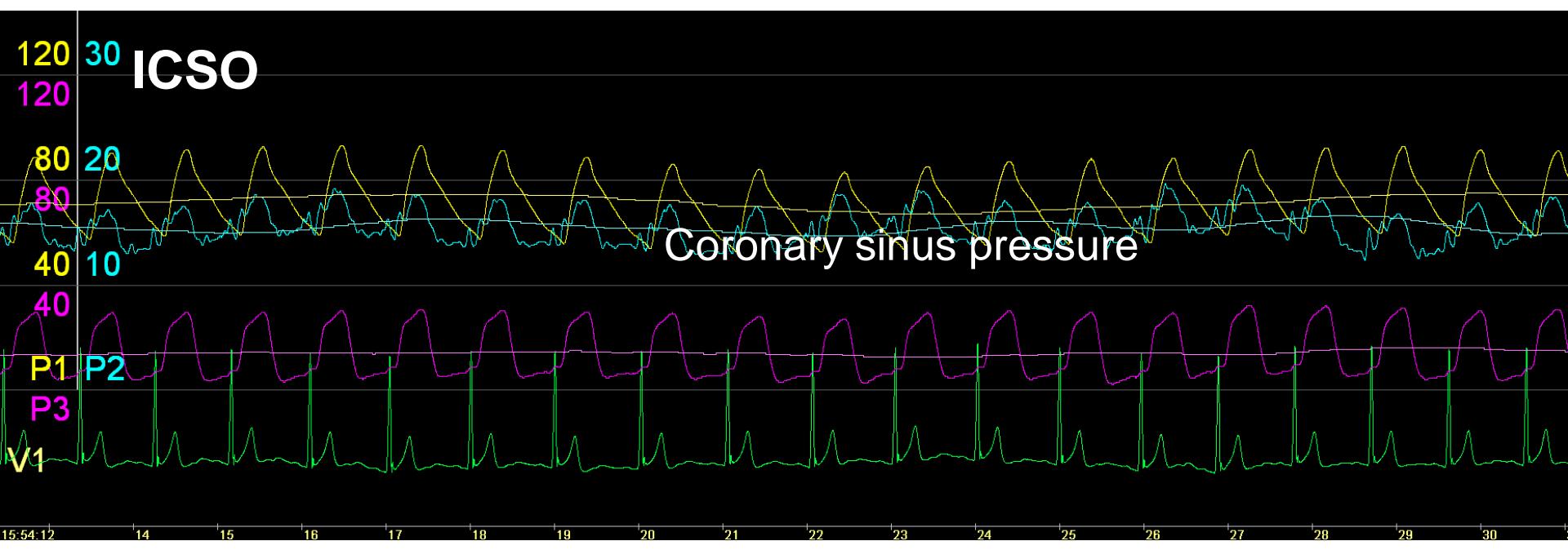
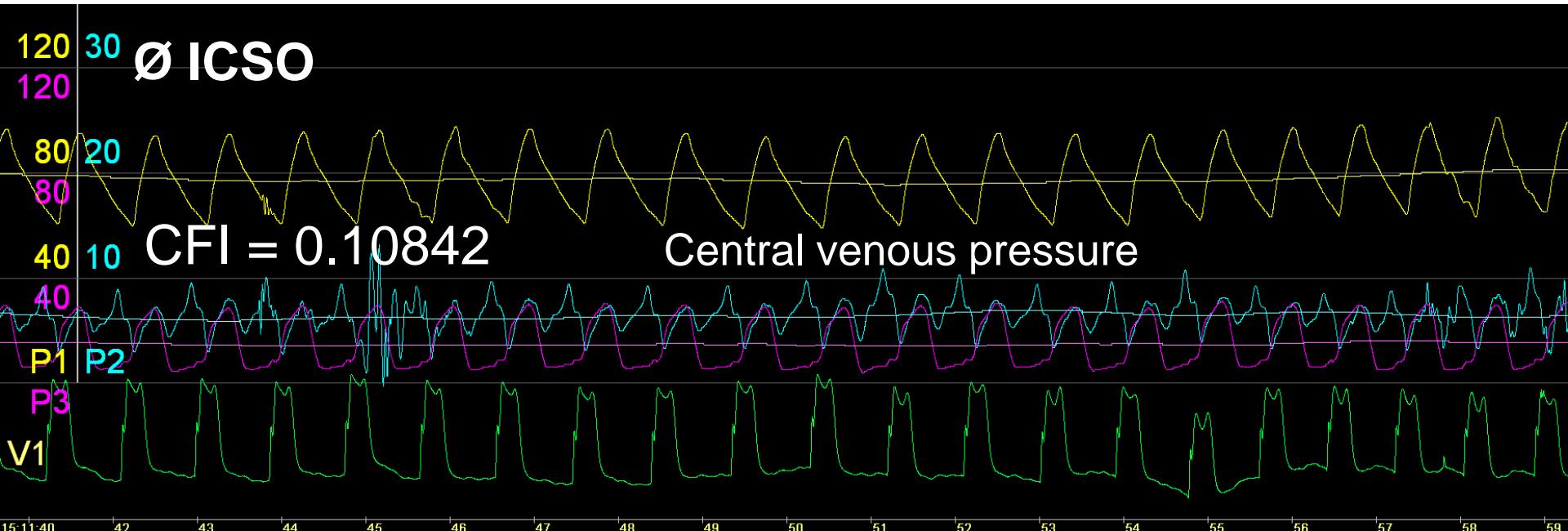
Placebo



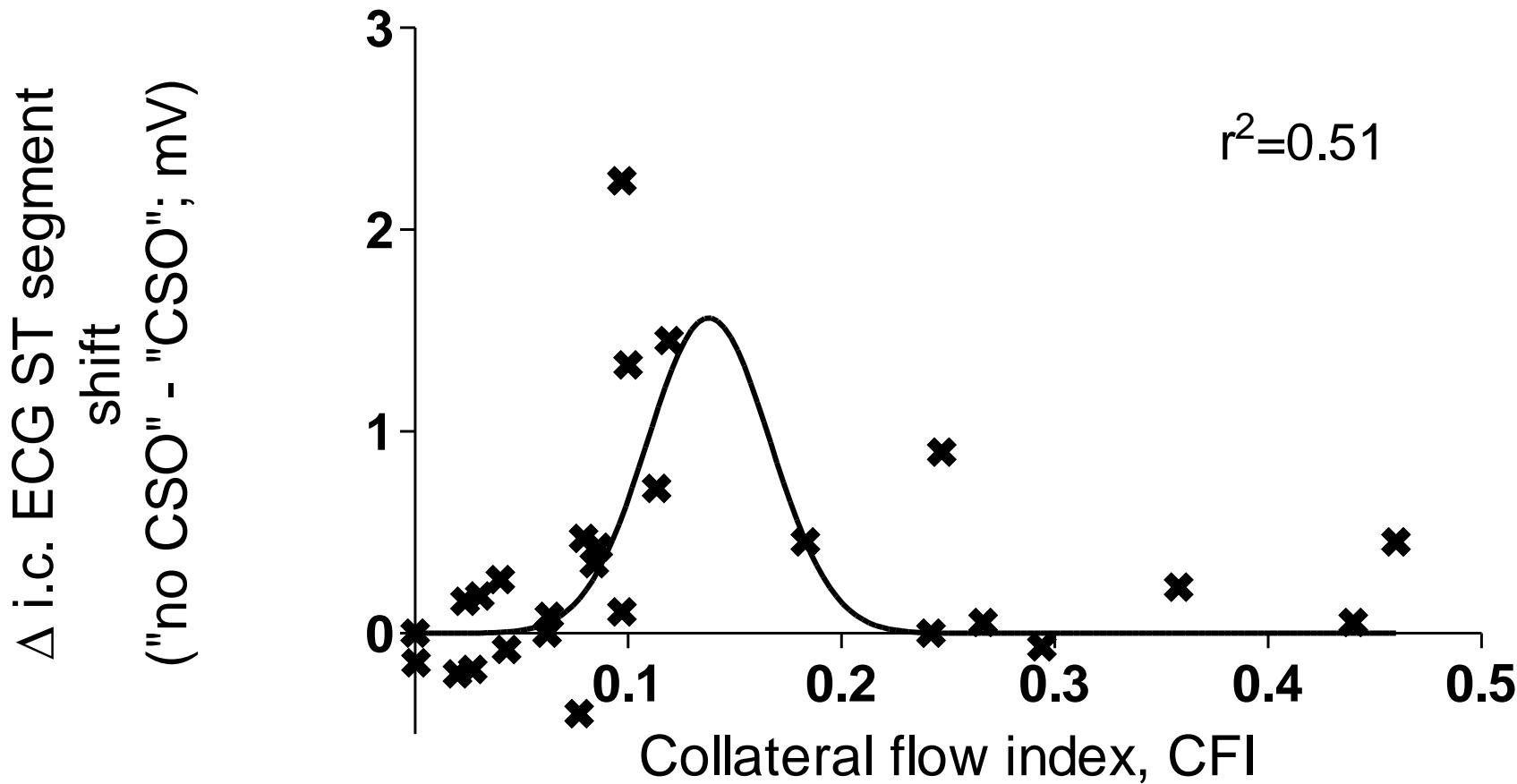


Effects of Coronary Sinus Occlusion on Intracoronary ECG ST Shift





Effects of Coronary Sinus Occlusion on Intracoronary ECG ST Shift

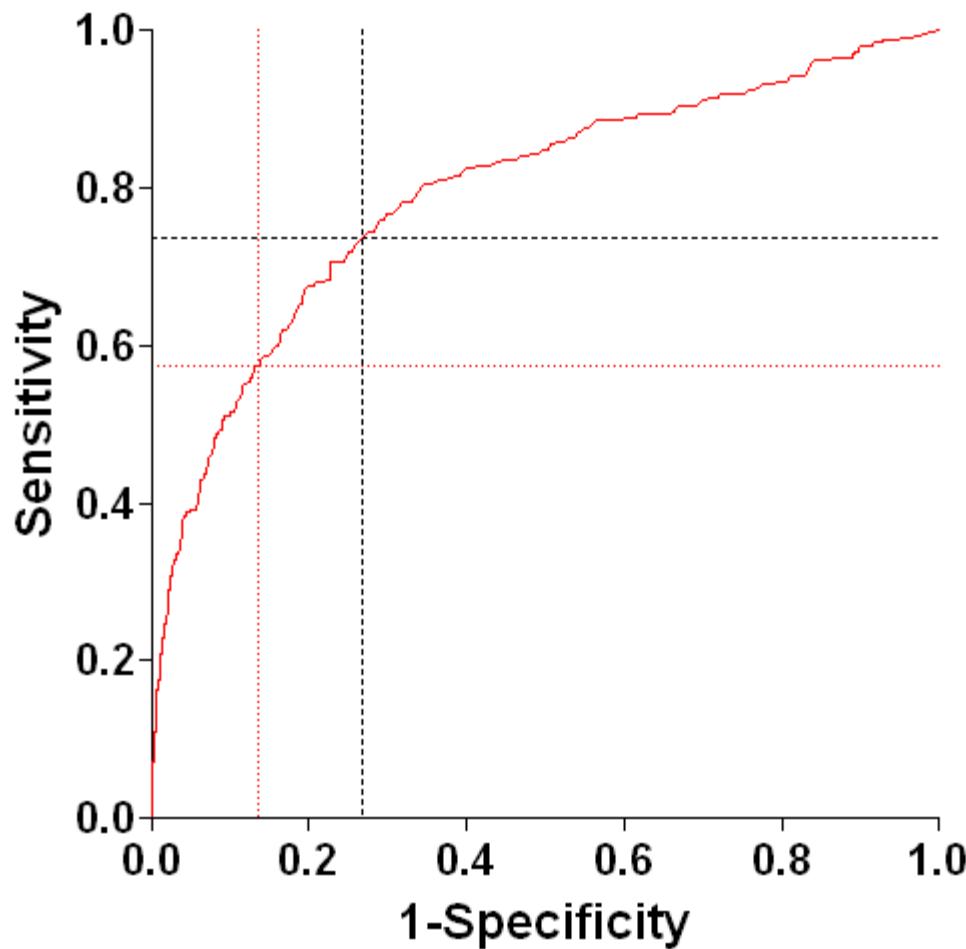


1896 Olympic Marathon



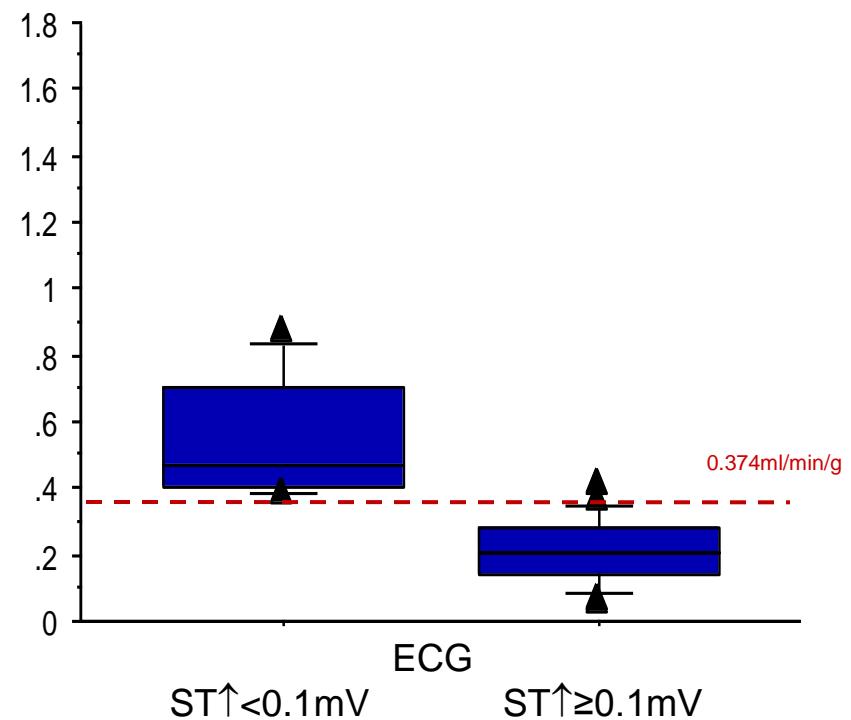
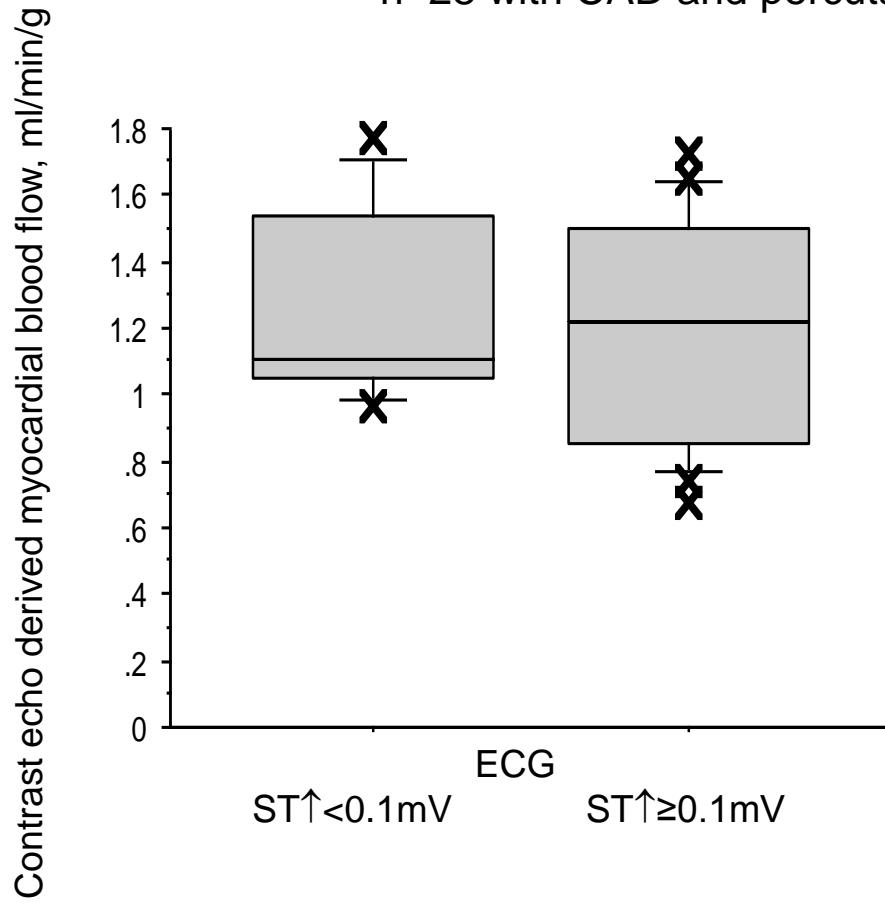
Spyridon Louis (GR): 2:58:50

I.c. ECG ST-Shift for the Detection of CFI > 0.200 (>0.250)



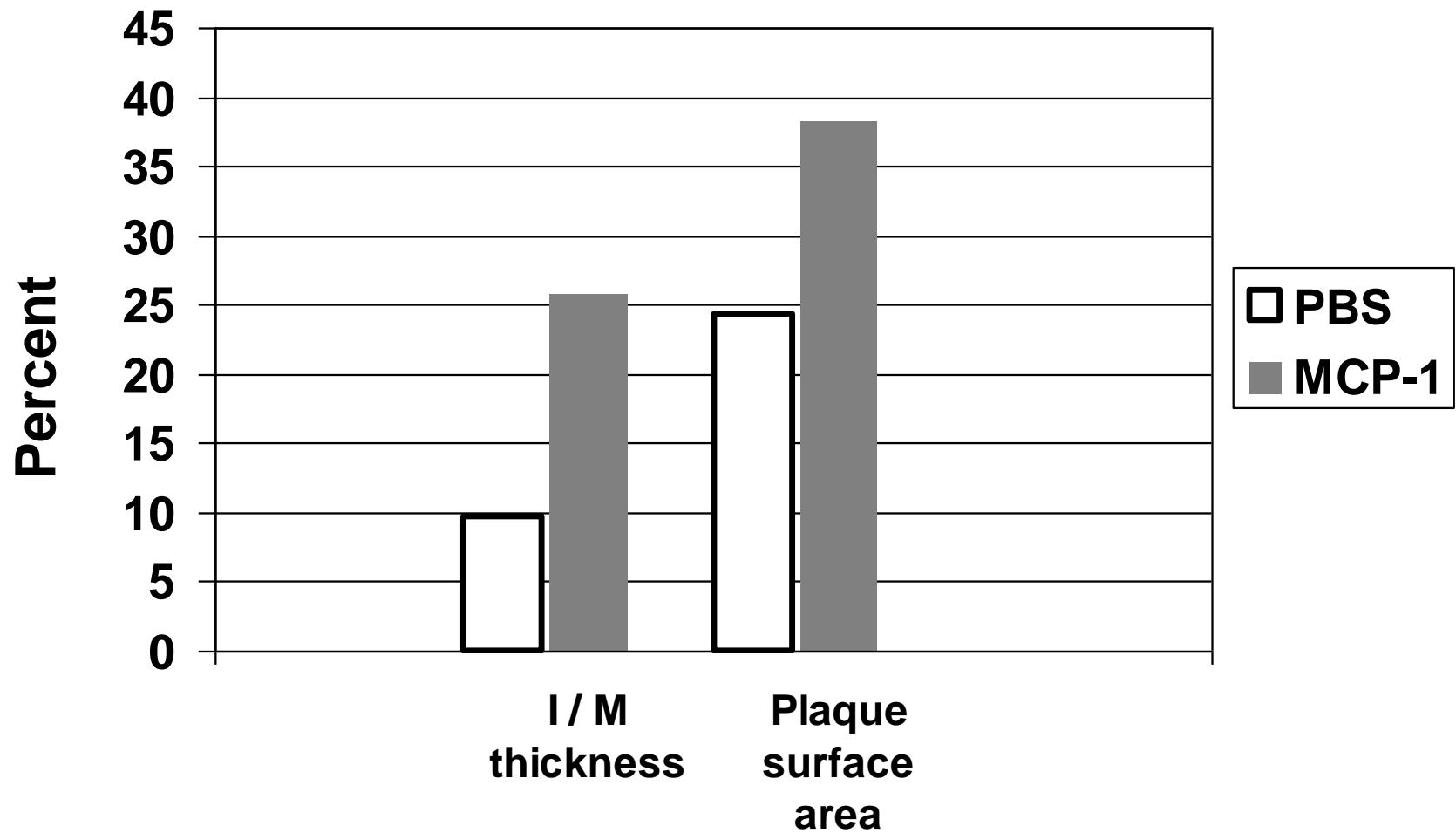
1-min Coronary Occlusion: ECG Signs of Ischemia and Myocardial Blood Flow

n=28 with CAD and percutaneous coronary intervention



Vogel et al. Heart 2007; 93: 115-

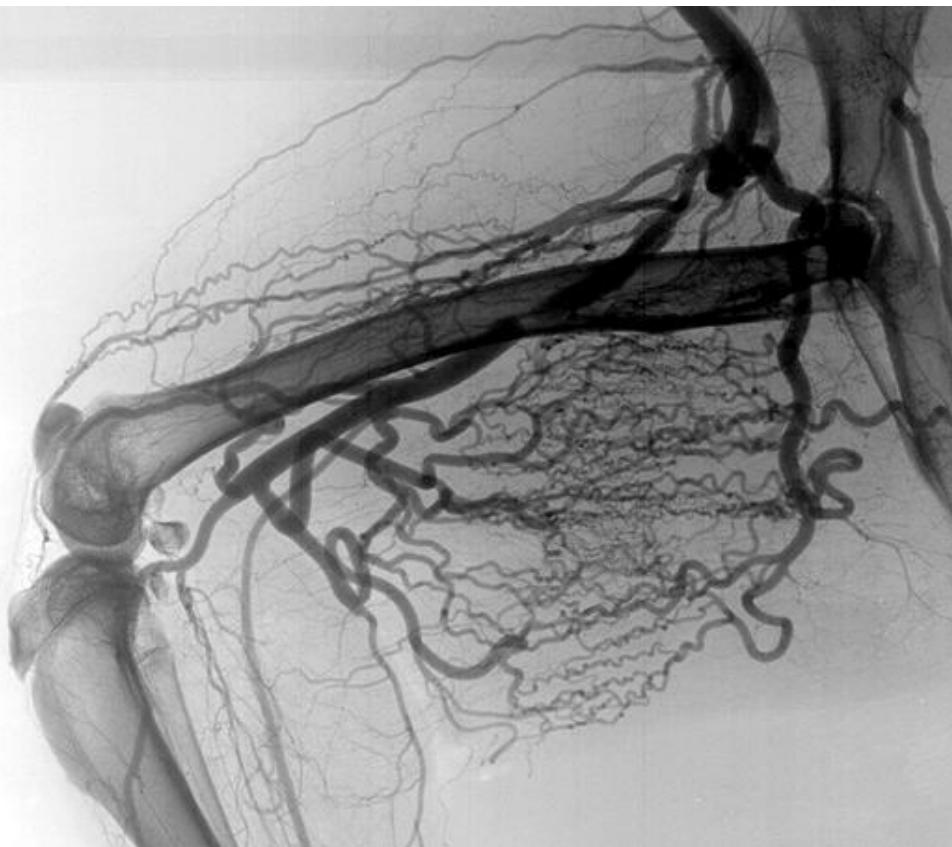
Hindlimb (Arterio-) and Atherogenesis in Apo-E^{-/-} Mice by MCP-1



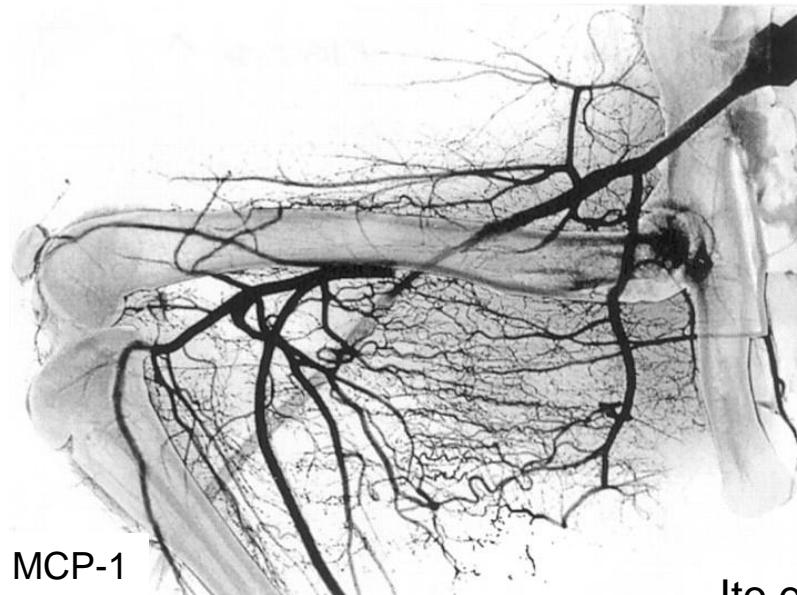
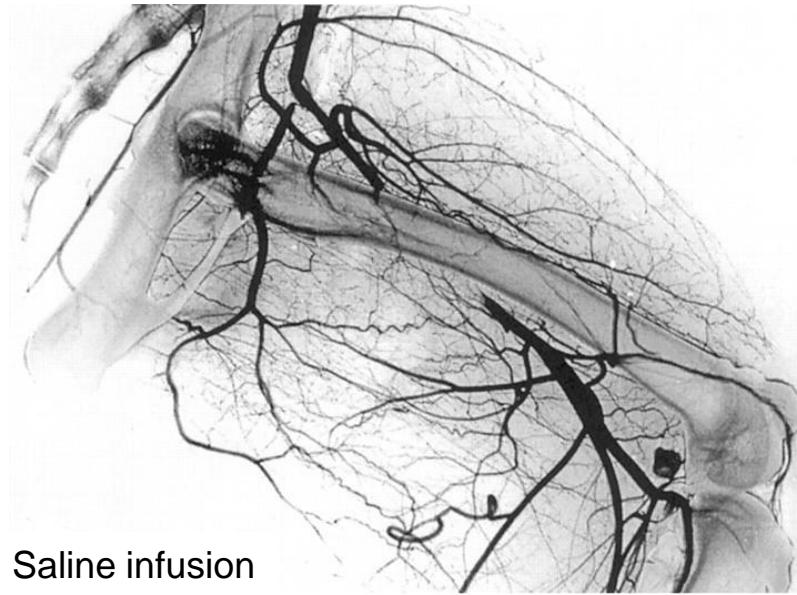
Femoral artery ligature



Ligature plus A-V shunt

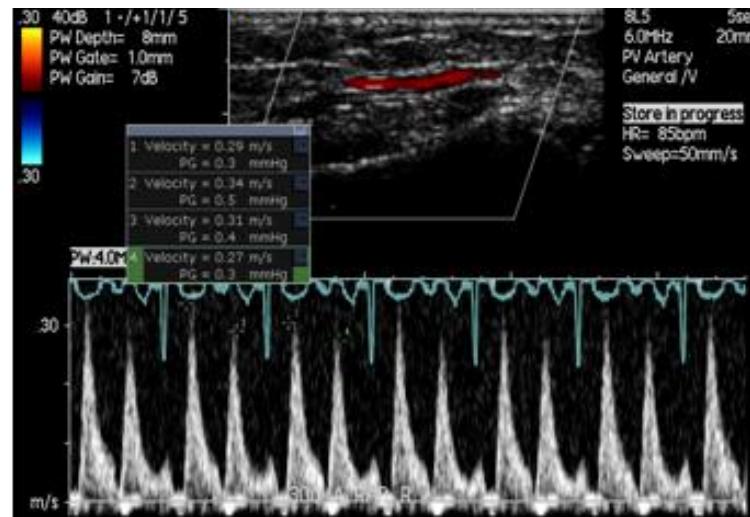
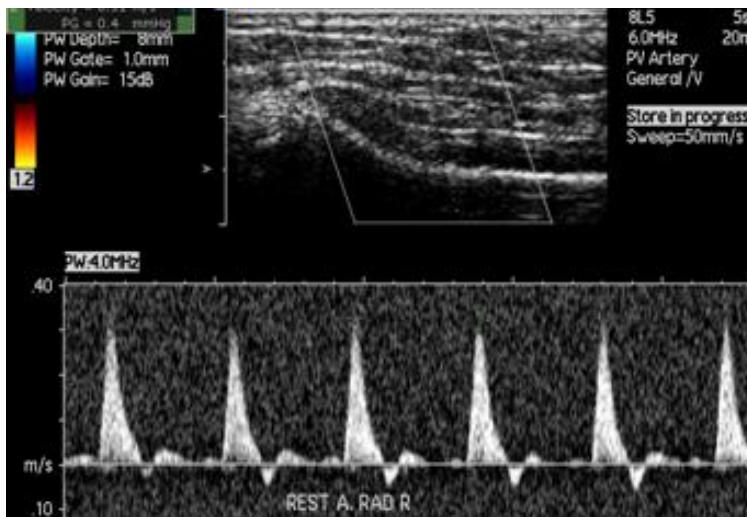
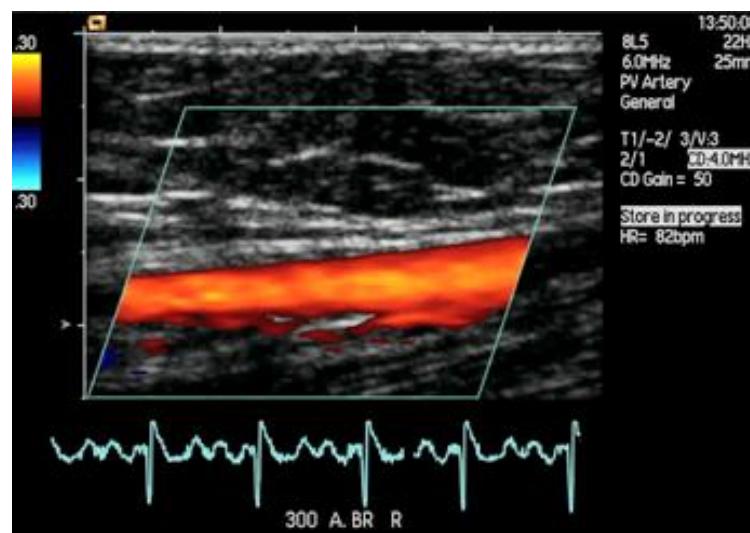


Hindlimb Arteriogenesis in Rabbits by Monocyte Chemotactic Protein-1

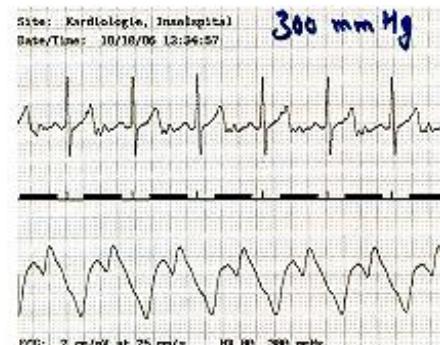
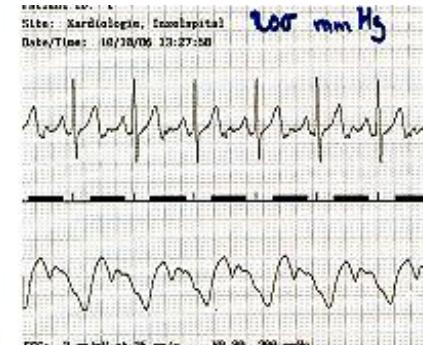
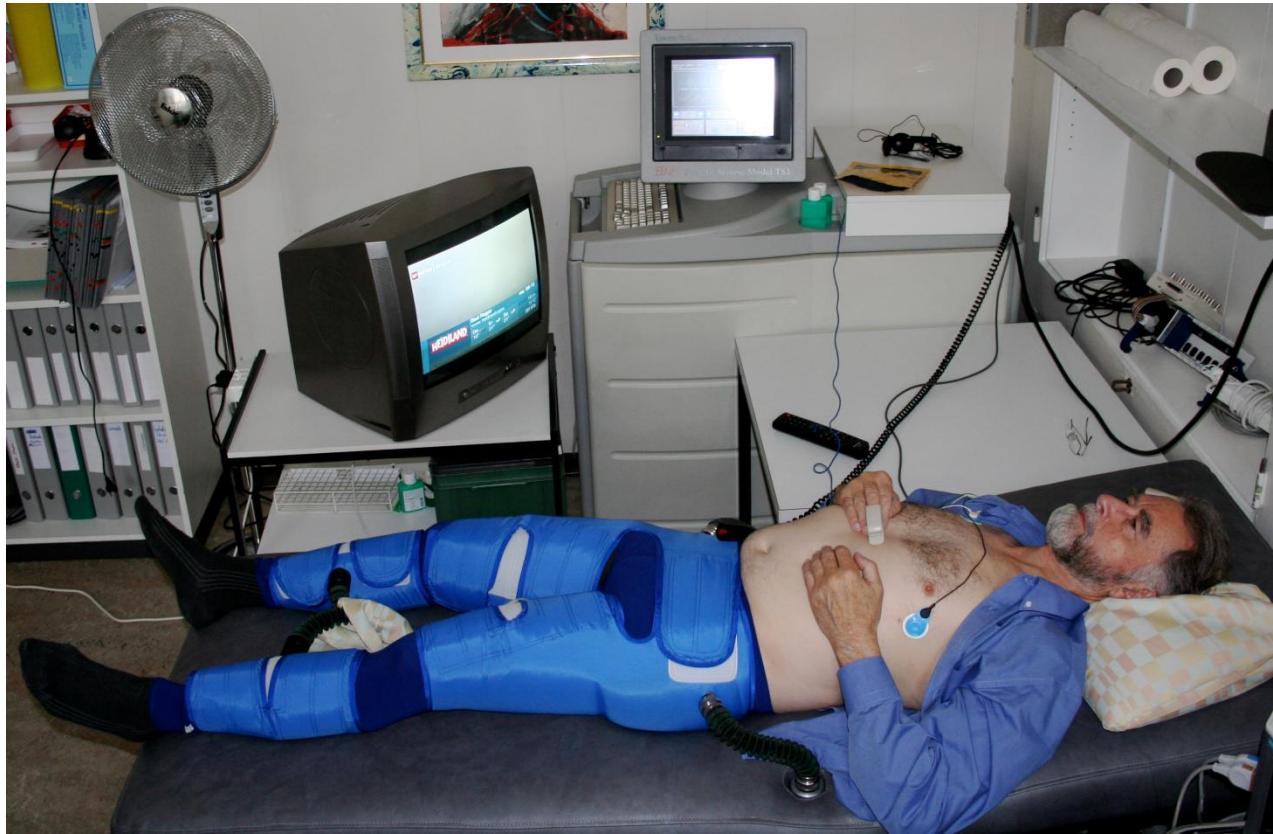


Ito et al. Circ Res 1997; 80: 829-

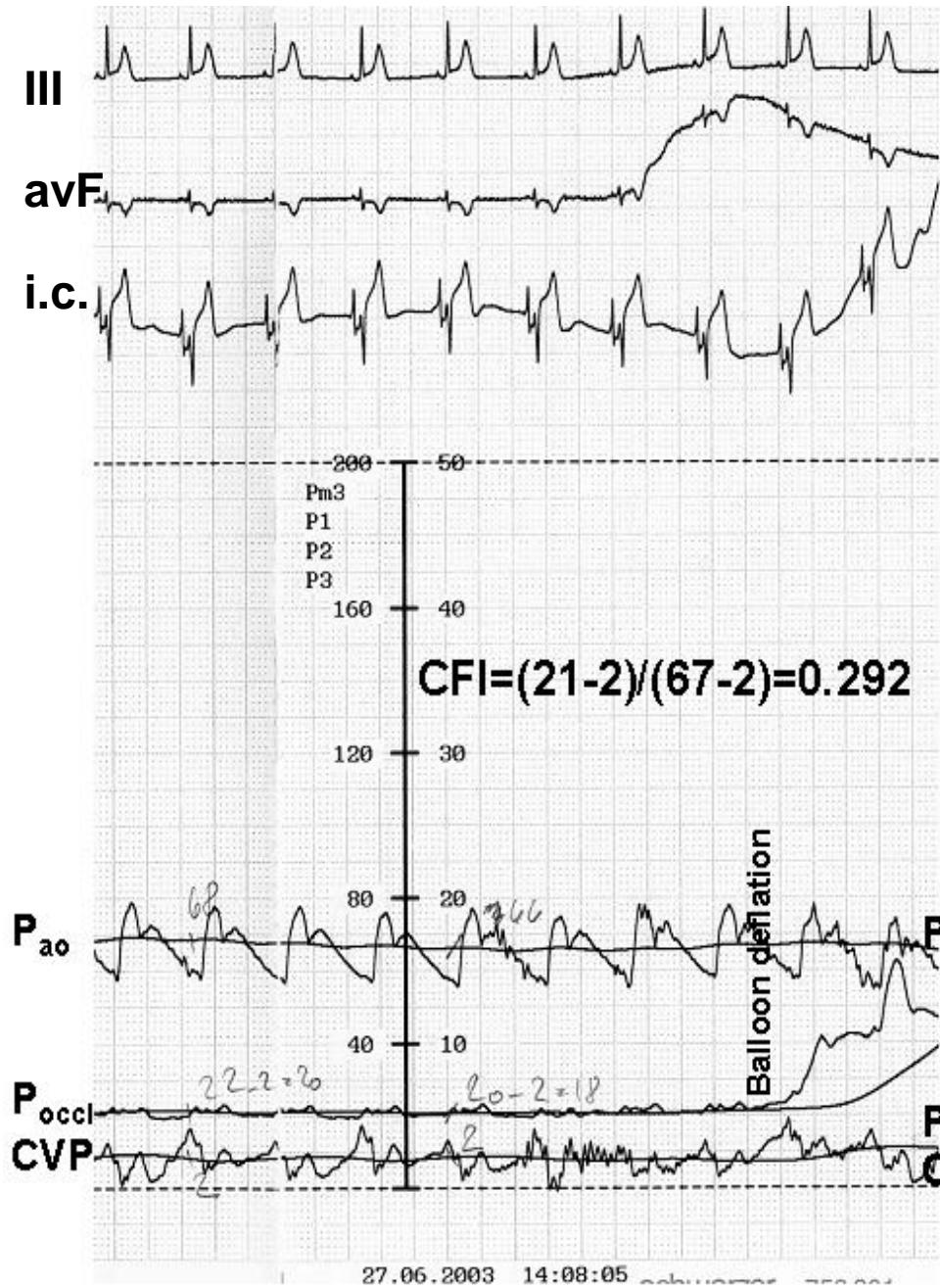
Diastolic augmentation of radial artery flow velocity



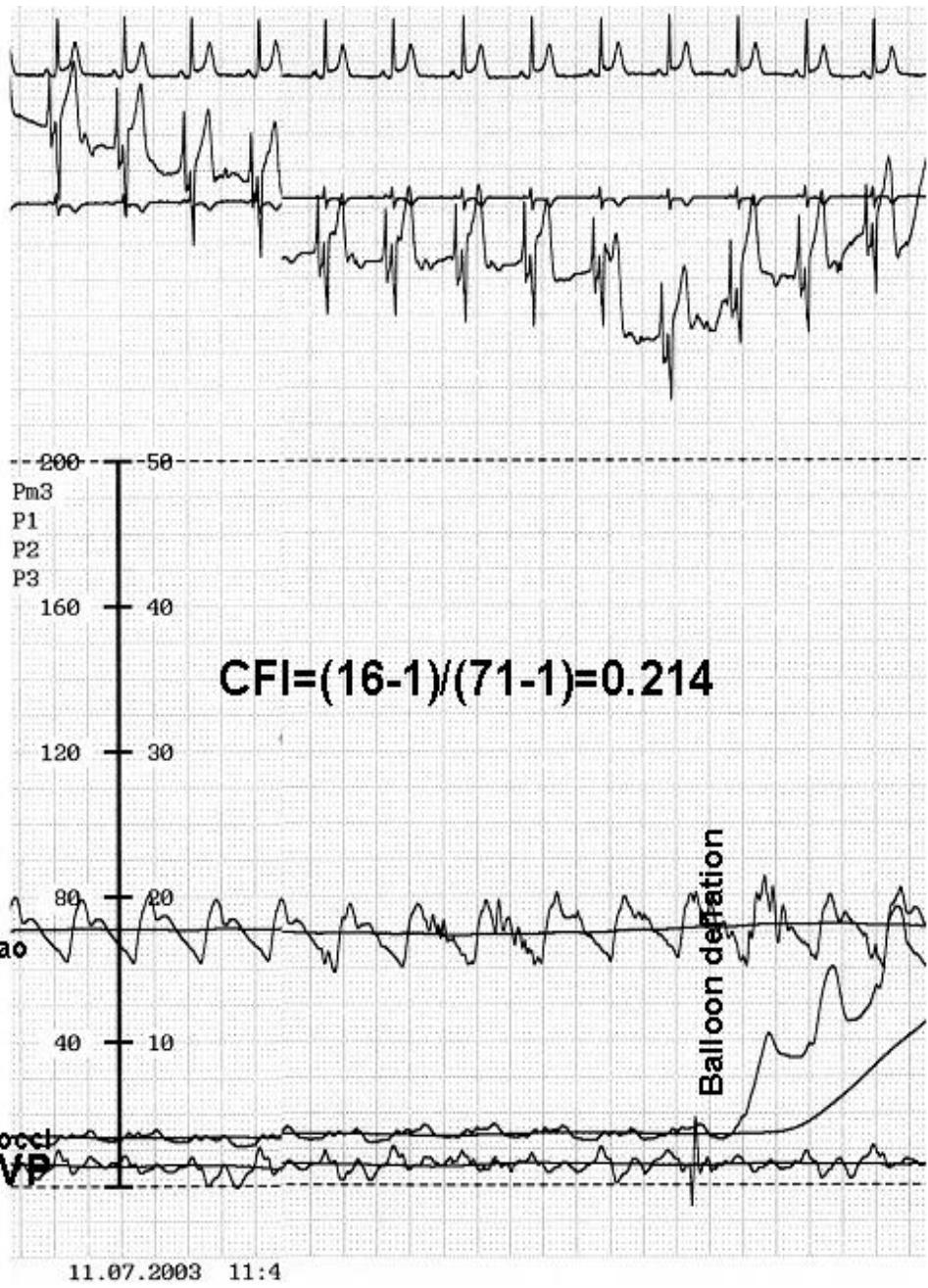
Increased Diastolic Coronary Shear Stress: External Counterpulsation



Before placebo treatment

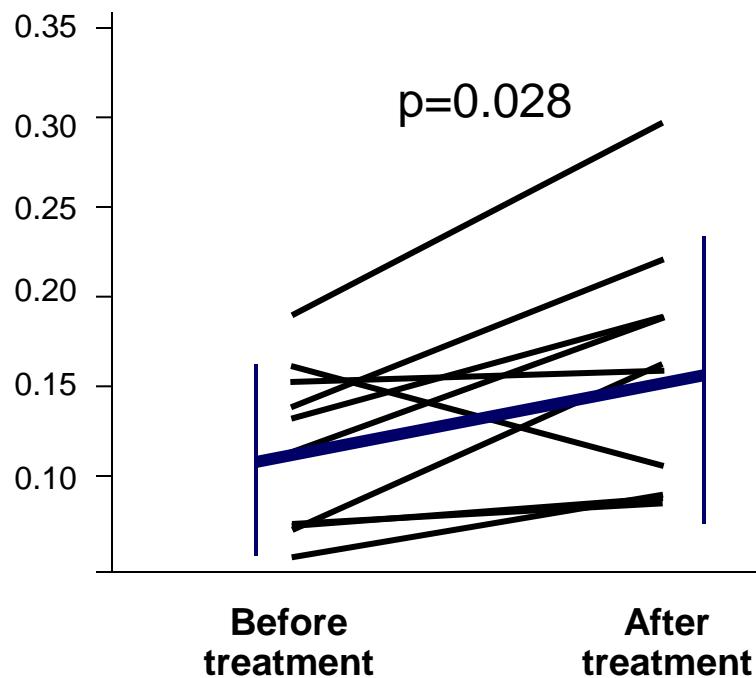


After placebo treatment

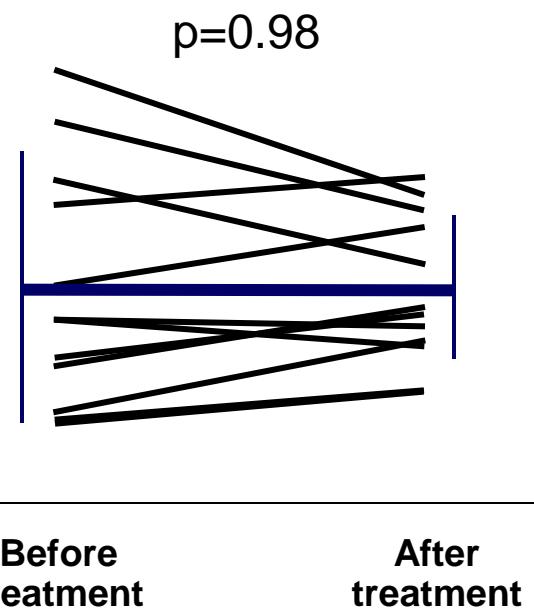


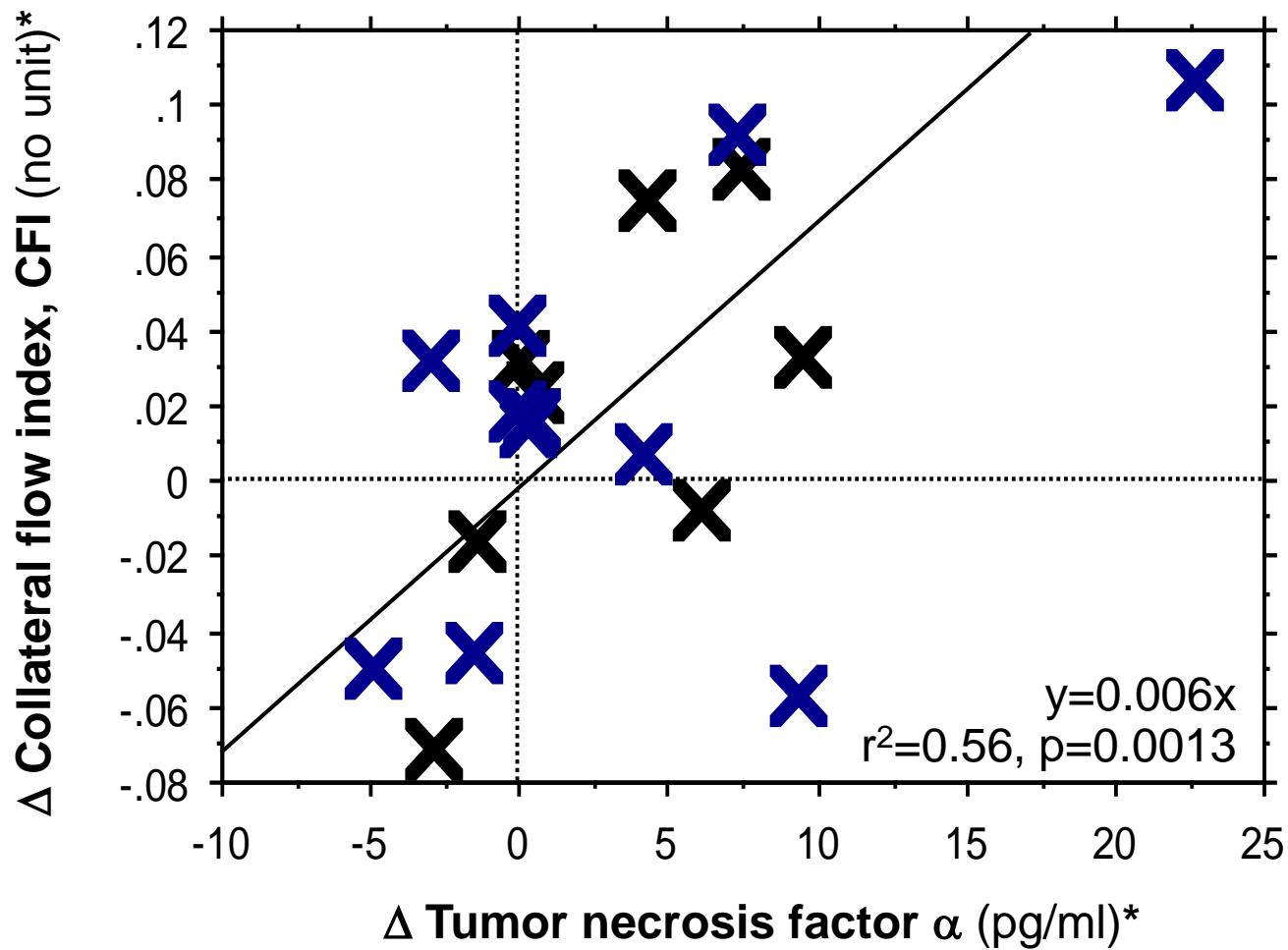
Collateral flow index, CFI (no unit)

GM-CSF



Placebo

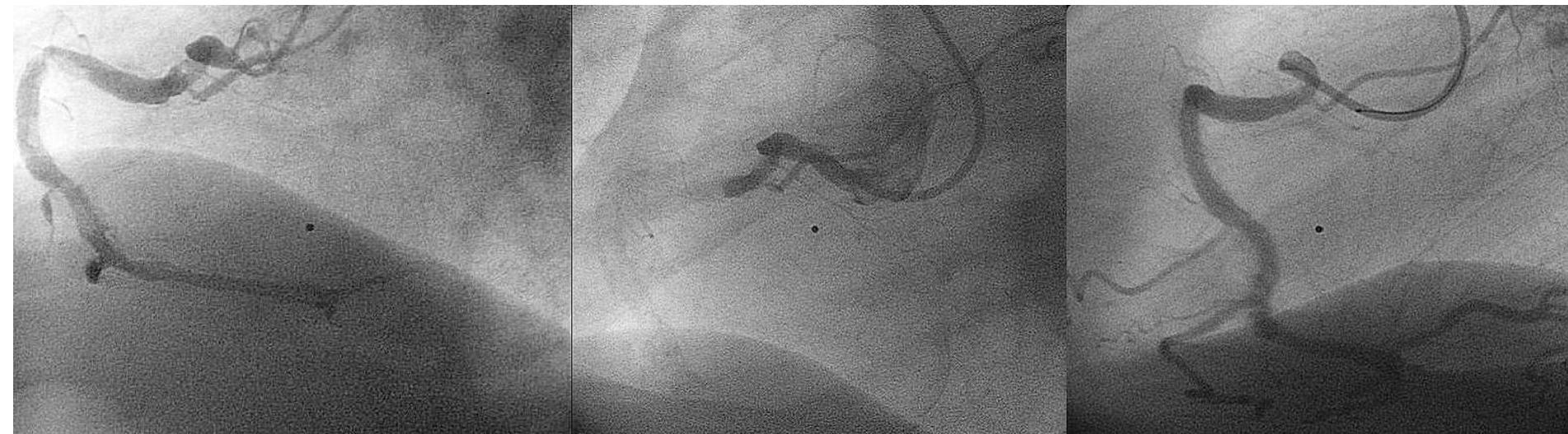


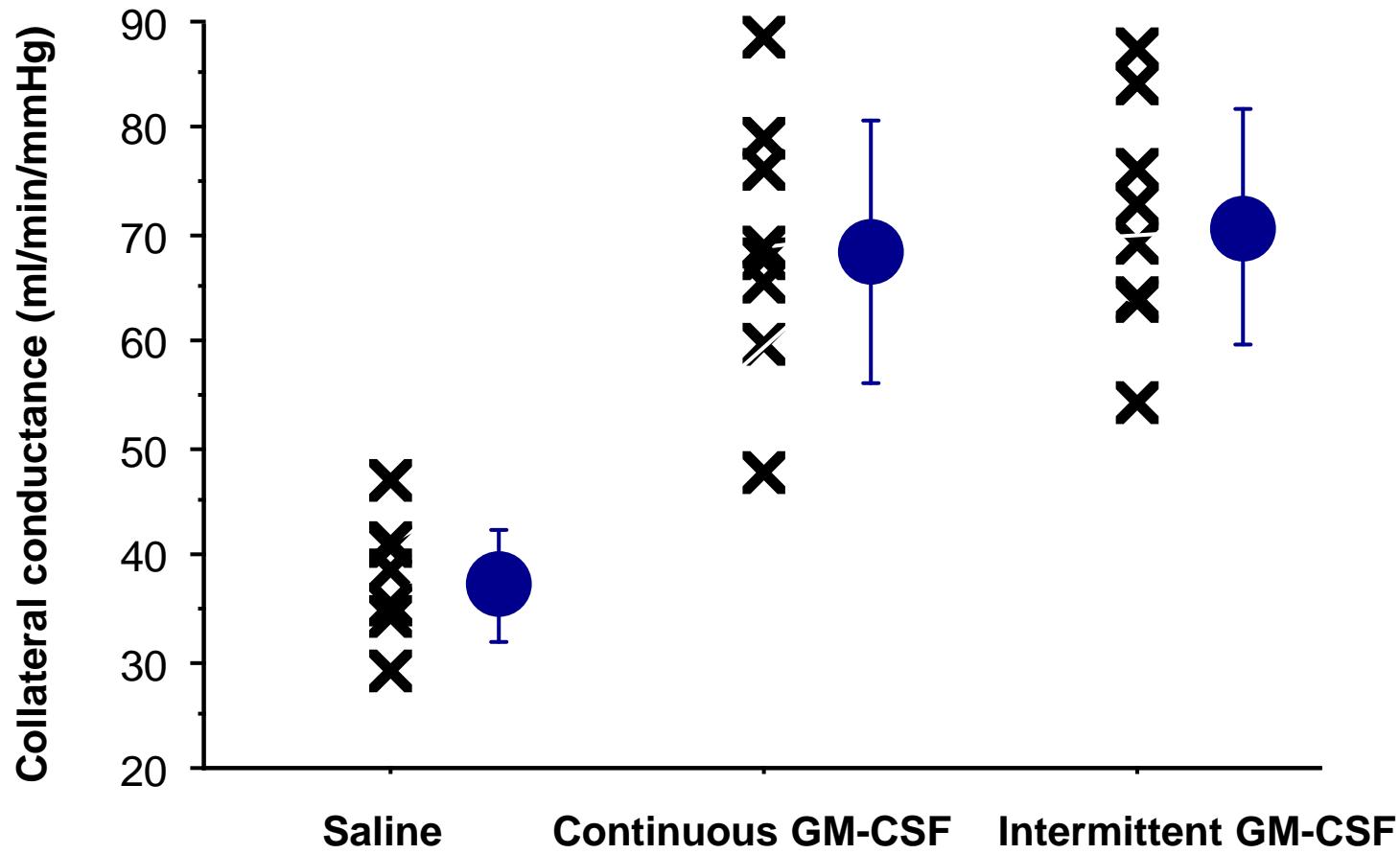


Day 0

Day 9

Day 9

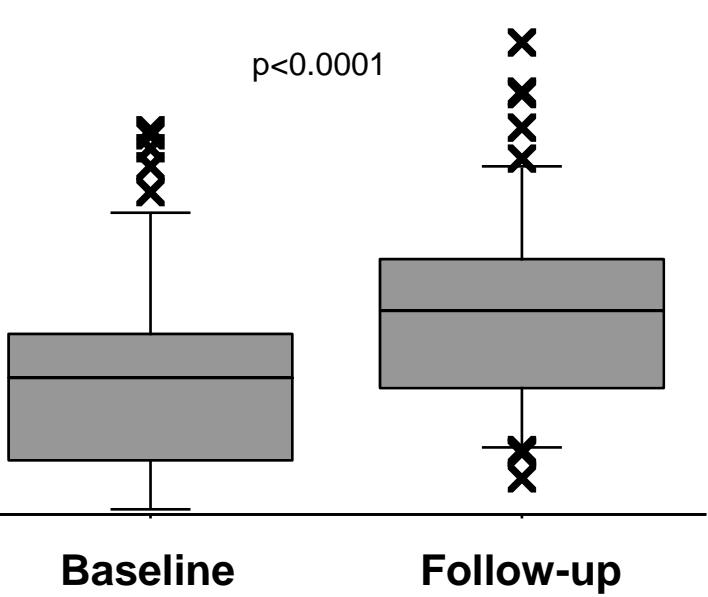




Collateral flow index (no unit)

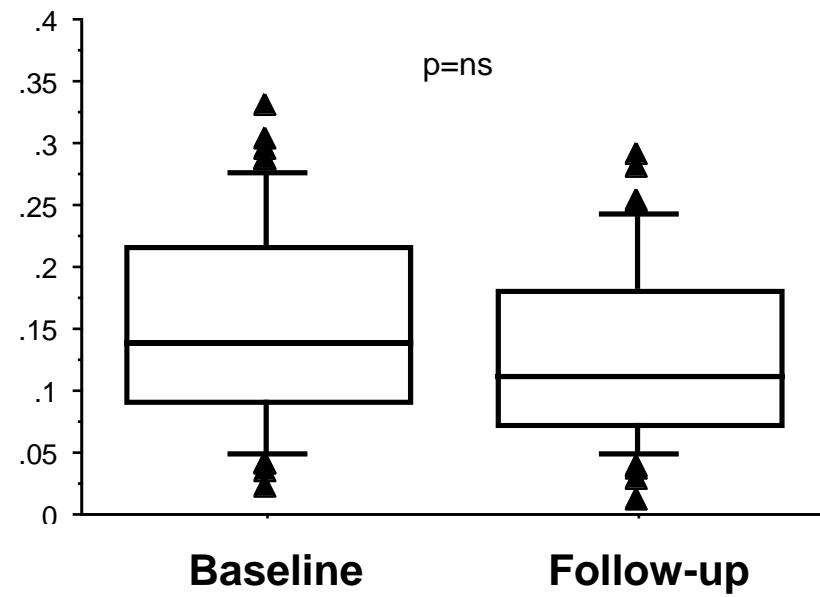
G-CSF

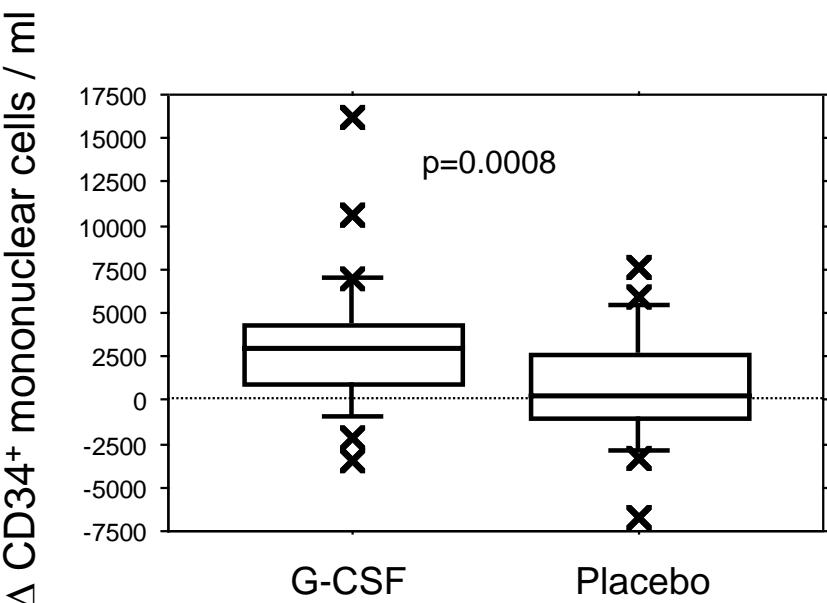
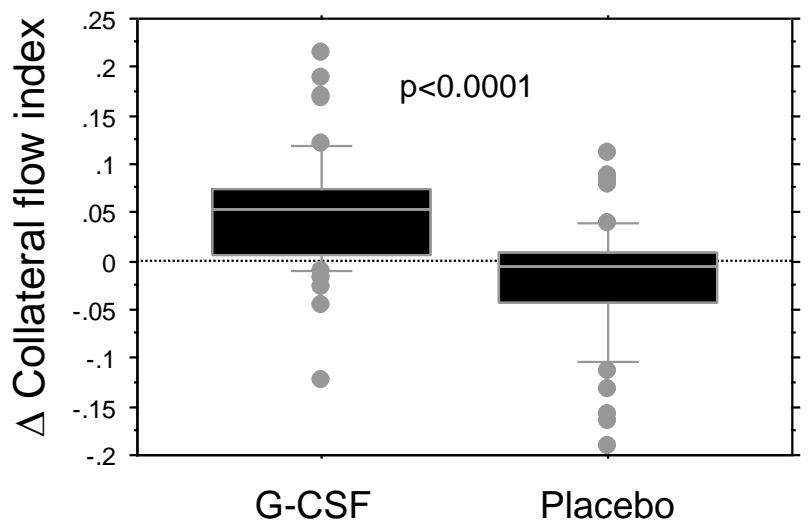
$p<0.0001$

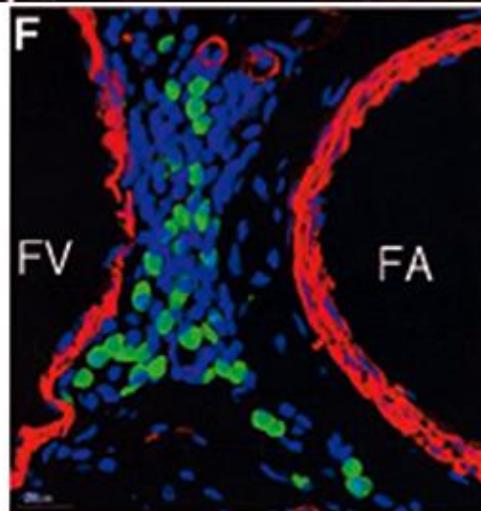
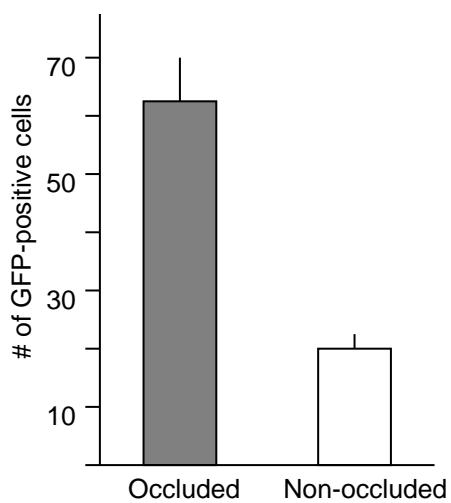
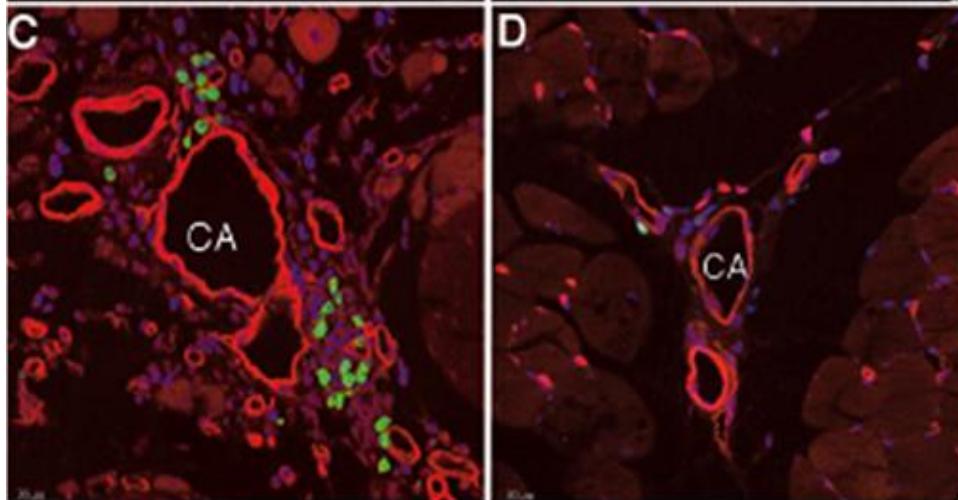
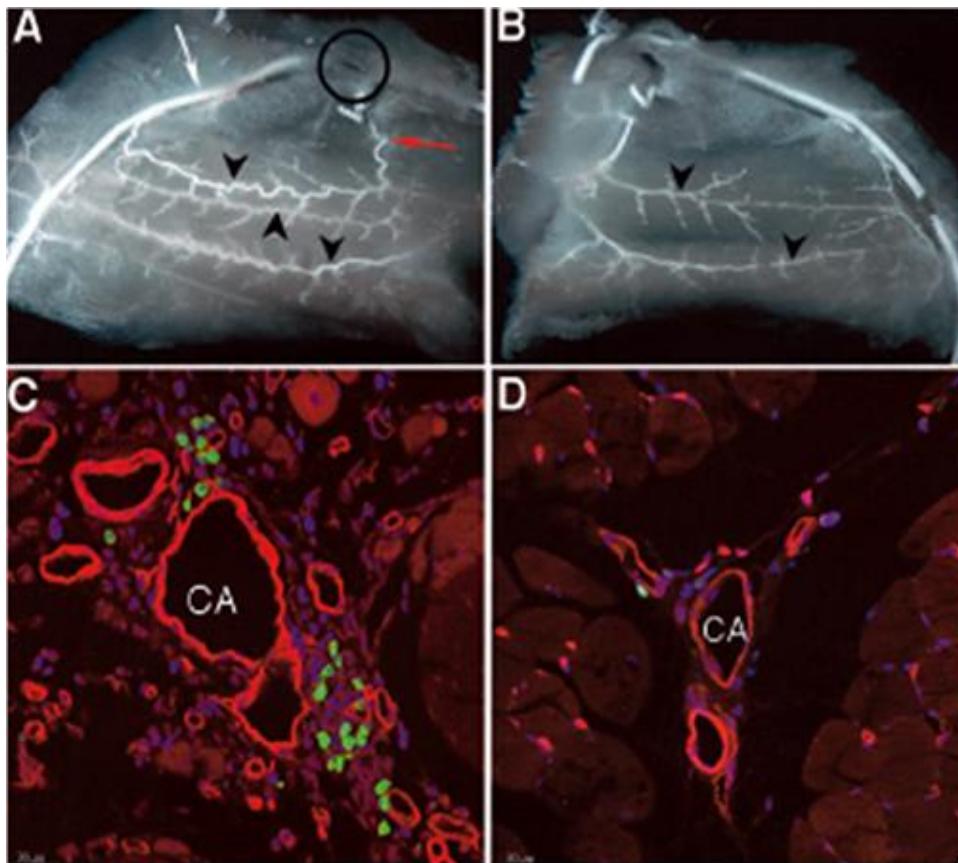


Placebo

$p=ns$









(a)



(b)



(c)



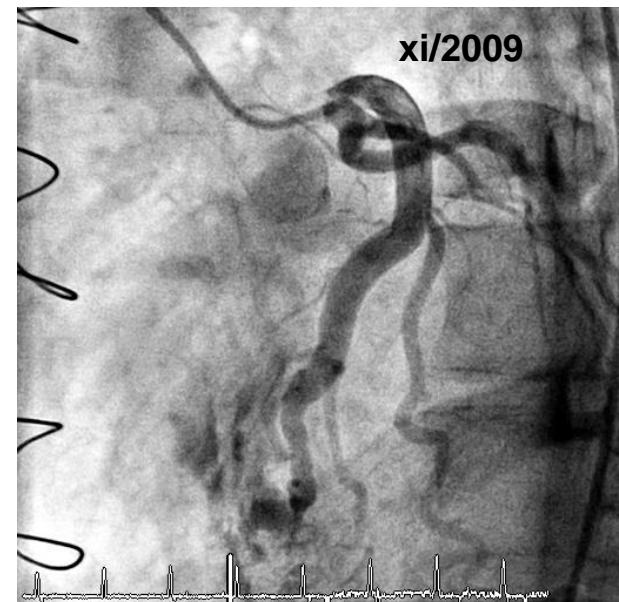
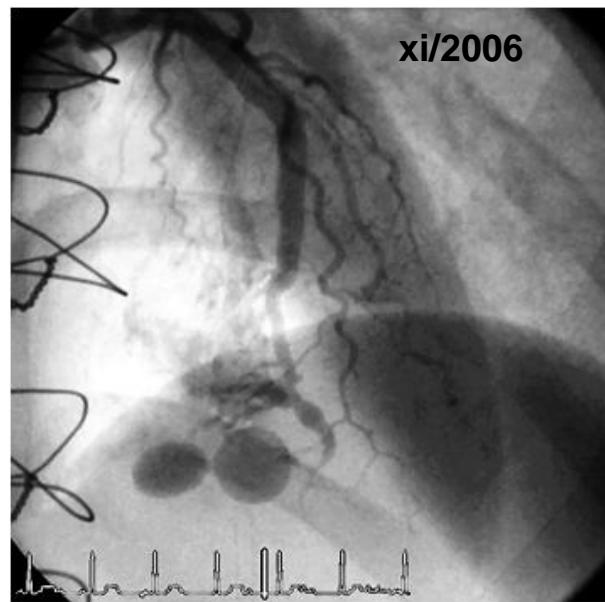
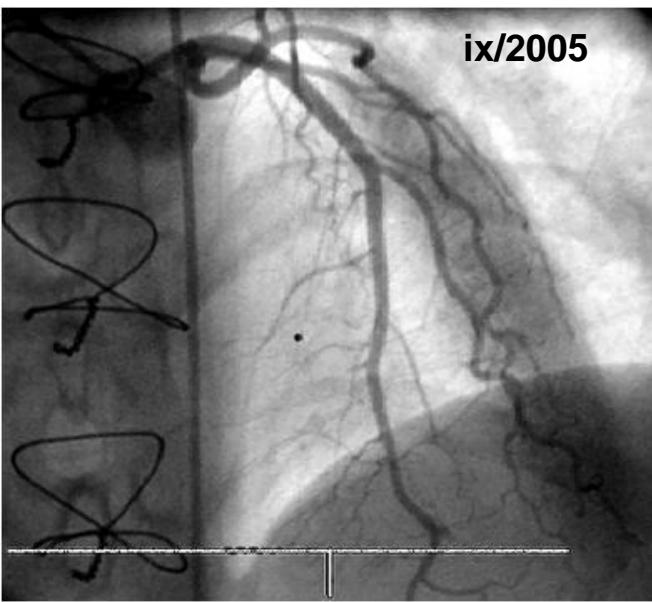
(d)



(e)

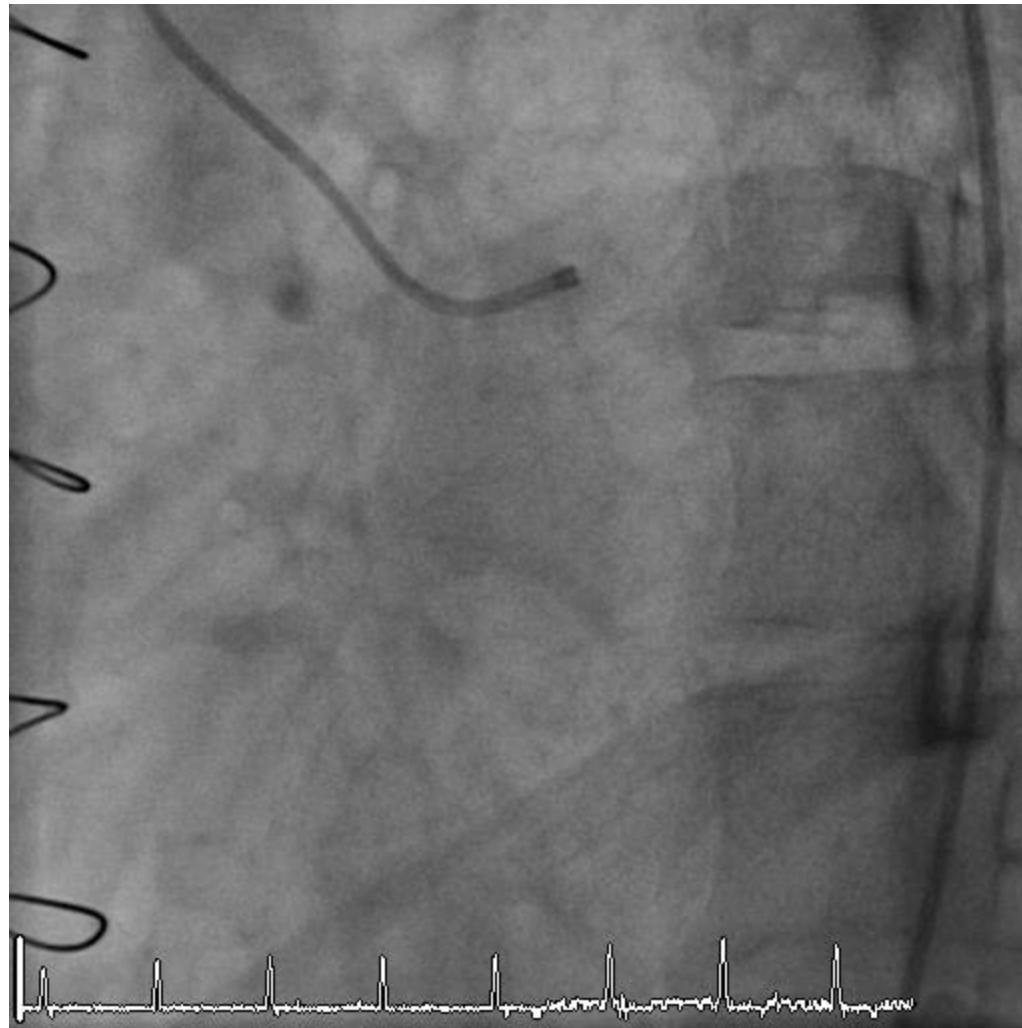


(f)

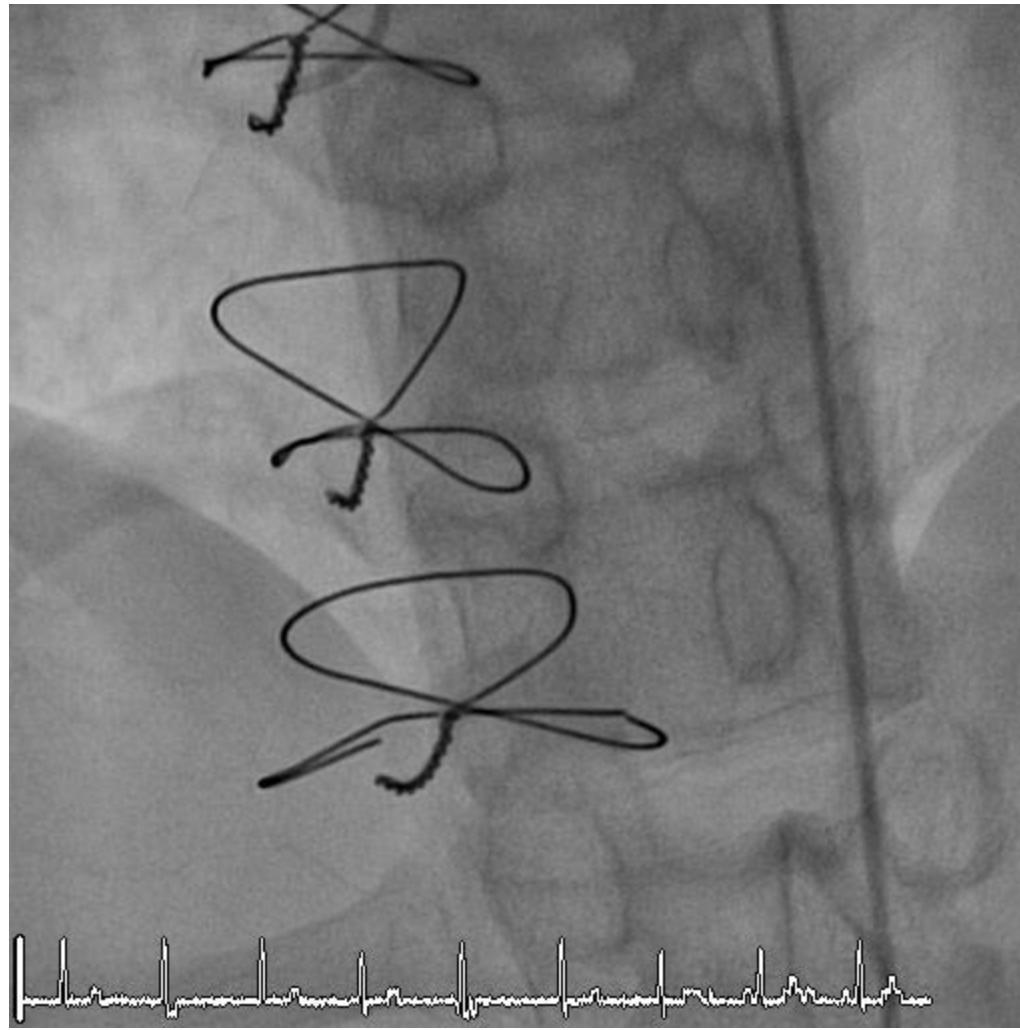


Vogel et al. Trends Cardiovasc Med 2010; 20: 129-

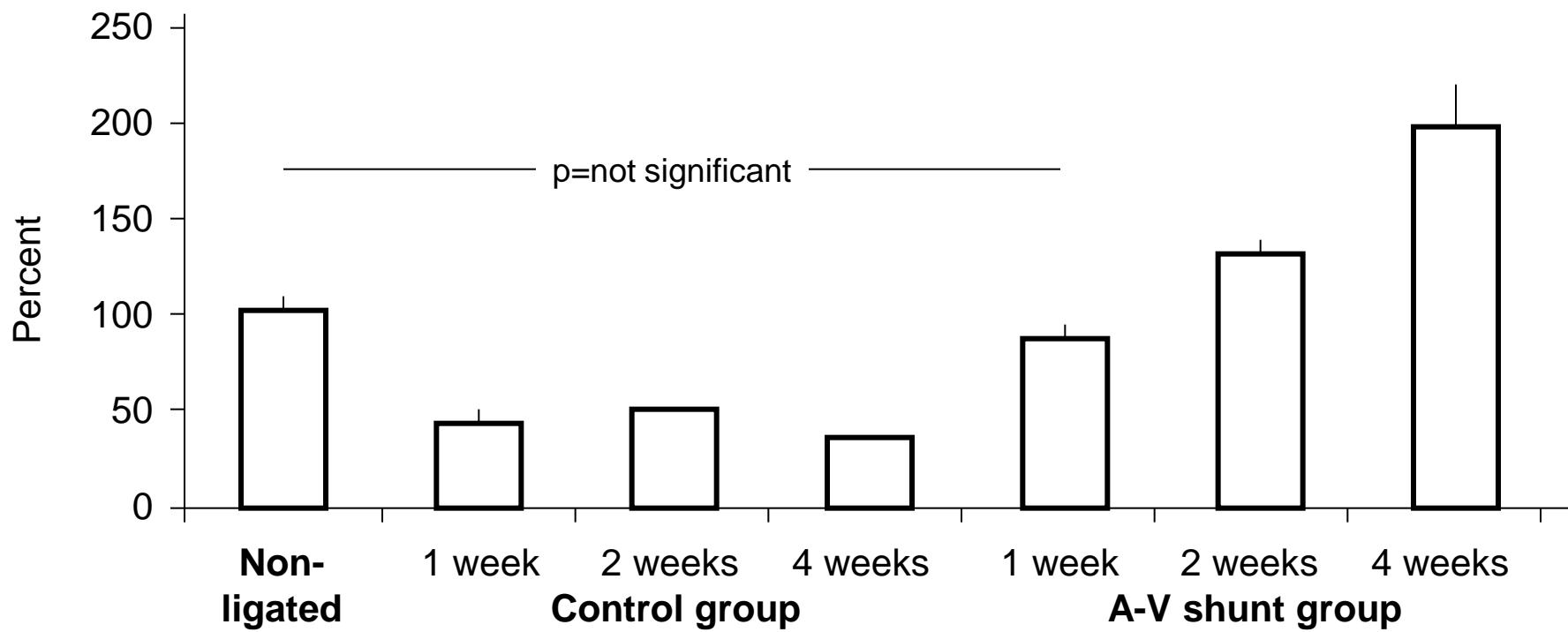
November 2009



November 2009



Collateral Conductance After Femoral Artery Ligature + A-V Shunt

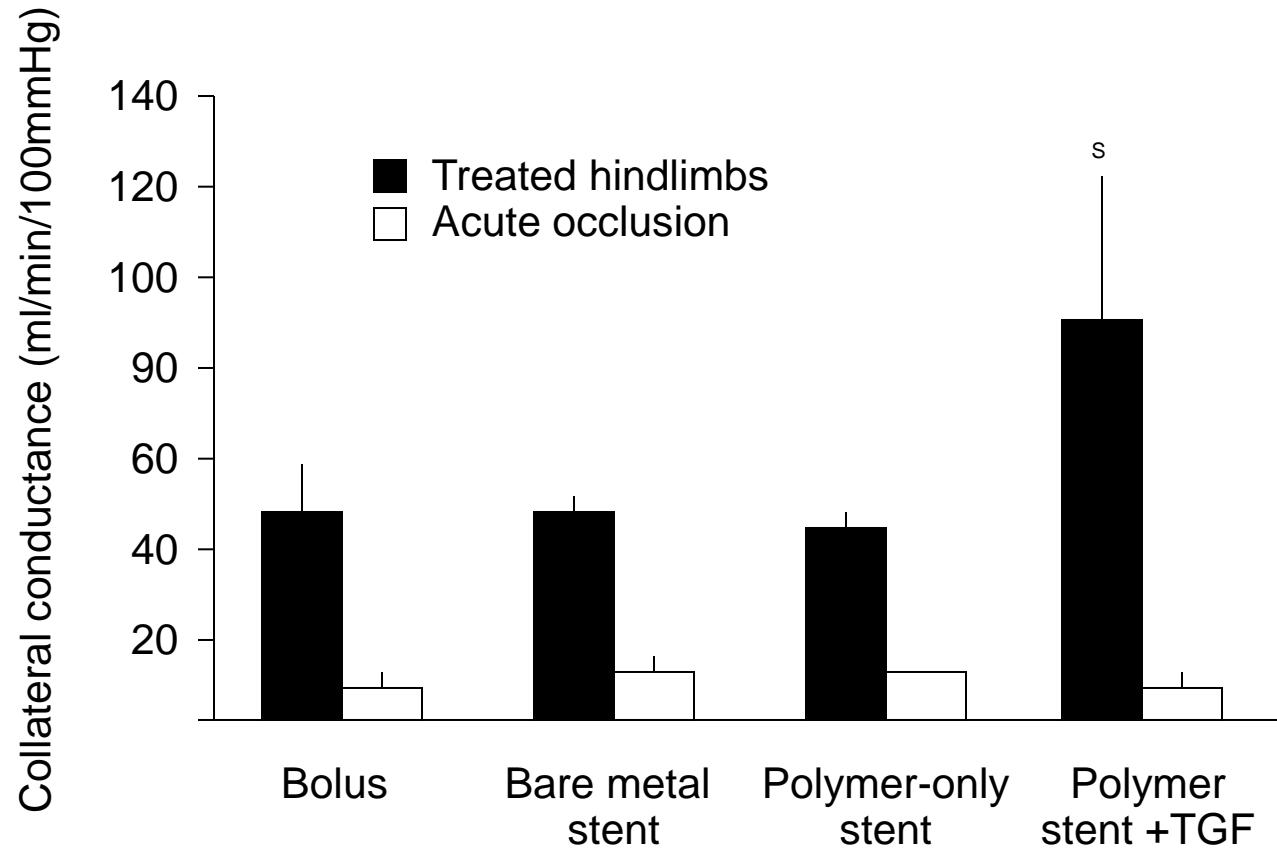


Eitenmüller et al. Circ Res 2006; 99: 656-

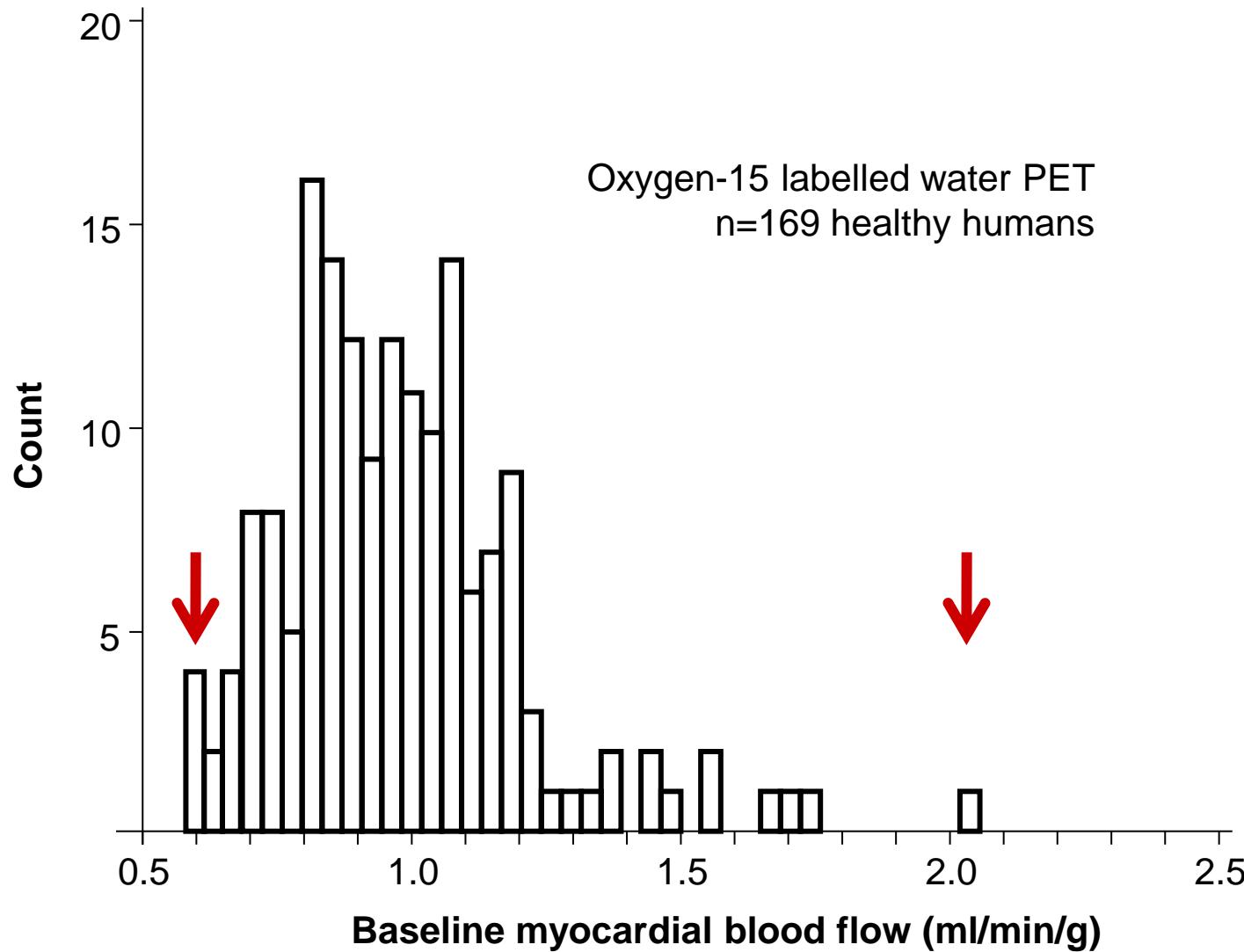
Physical Coronary Arteriogenesis

- Arteriogenesis = structural artery growth
- \uparrow Flow velocity: trigger for arteriogenesis
- \uparrow Flow velocity due to \uparrow pressure gradient
- Process in native and collateral arteries
- Arterio-venous shunt: model for arteriogenesis
- A-V shunt creation: arteriogenesis progression
- A-V shunt closure: arteriogenesis regression
- Implication: \uparrow diastolic flow velocity / duration

Hindlimb Arteriogenesis in Rabbits by Transforming Growth Factor- β 1



Baseline Myocardial Perfusion by PET



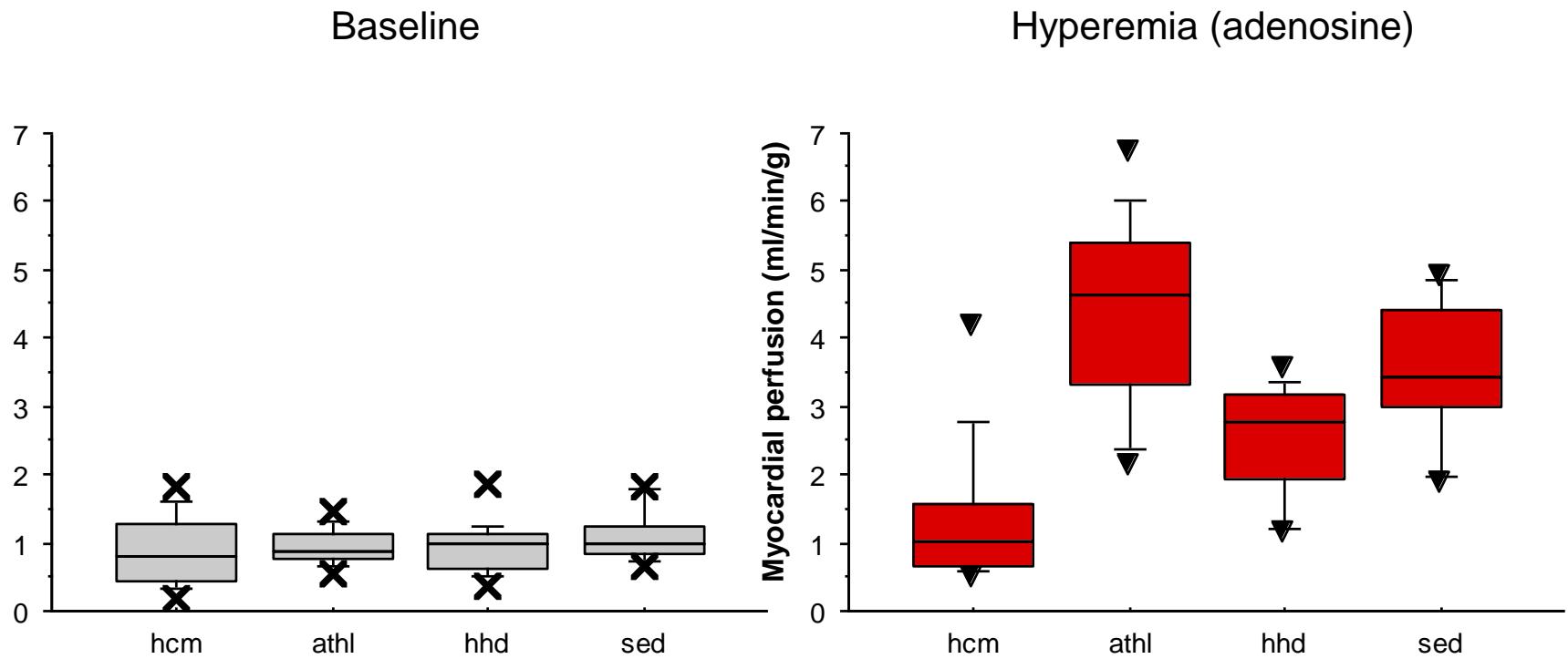
Chareonthaitawee et al. Cardiovasc Res 2001; 50: 151-

Myocardial Perfusion by Contrast Echo



Vogel et al. J Am Coll Cardiol 2005; 45: 754-

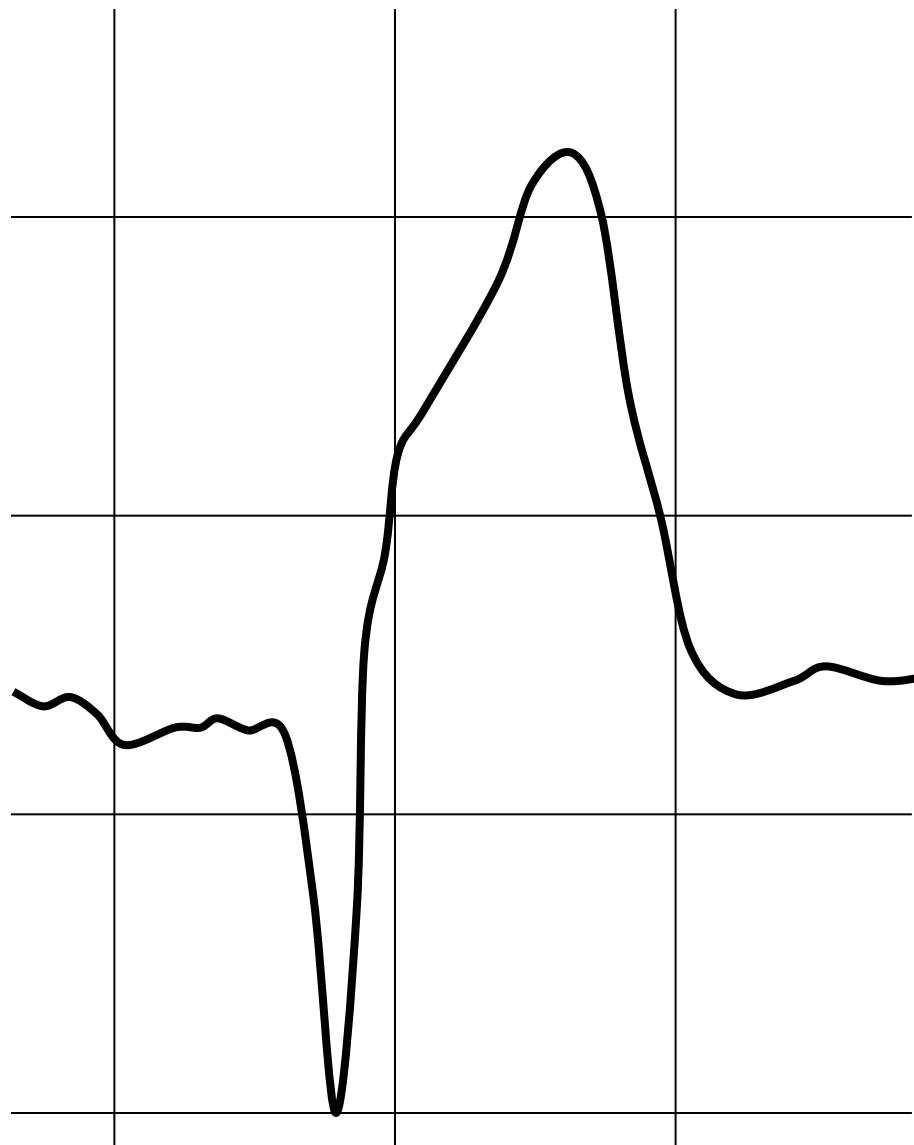
Baseline and Hyperemic Myocardial Perfusion by Contrast Echo



hcm hypertrophic cardiomyopathy
athl athlete's heart
hhd hypertensive heart disease
sed sedentary; normal heart

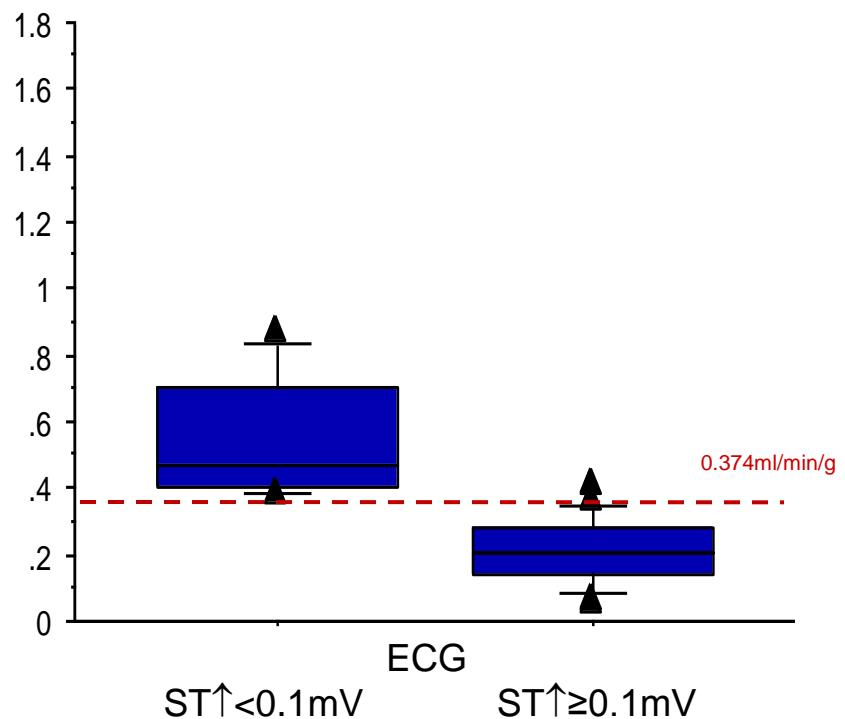
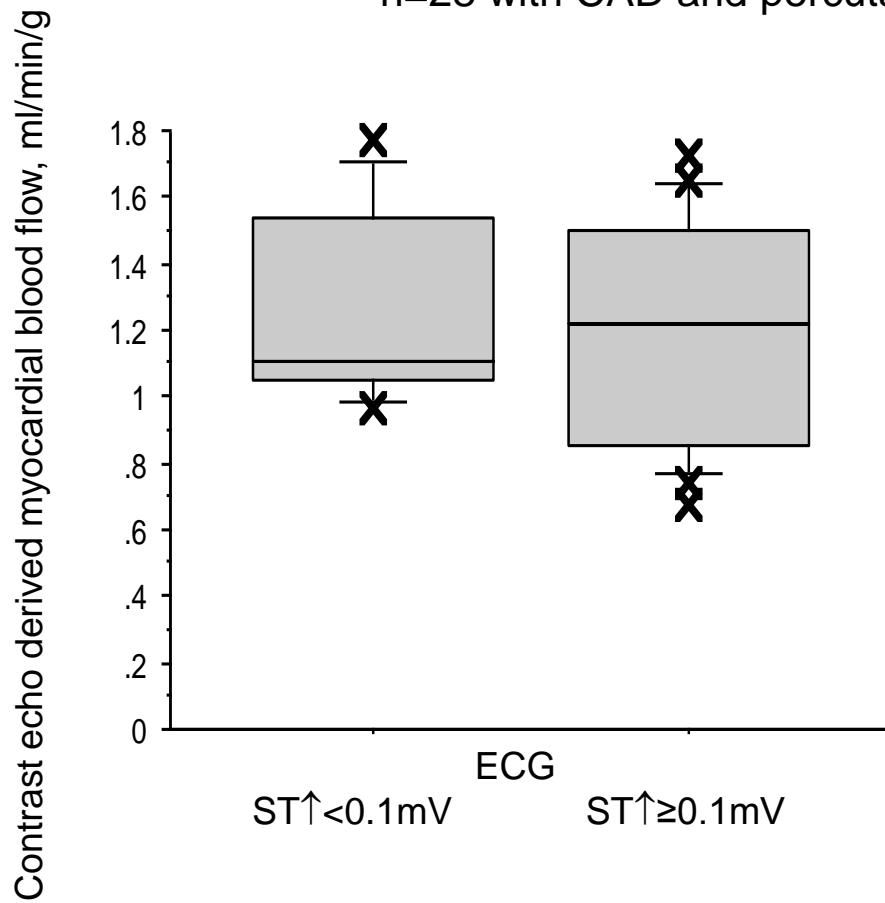
Indermühle et al. Eur Heart J 2006; 27: 1571-
Indermühle et al. SMW 2009; 139: 691-

Lower Limit of Myocardial Perfusion



1-min Coronary Occlusion: ECG Signs of Ischemia and Myocardial Blood Flow

n=28 with CAD and percutaneous coronary intervention



Vogel et al. Heart 2007; 93: 115-

Hindlimb Arteriogenesis in Rabbits by Monocyte Chemotactic Protein-1

